Evaluation of the Effectiveness of Anti-Special Coating on The Model of Lung Wound in The Experiment

Xujabaev S. T.[1]	Department of General Surgery[1] Samarkand State Medical University
Rajabov J. P.[1]	Department of General Surgery[1] Samarkand State Medical University
Dusiyarov M.M.[1]	Department of General Surgery[1] Samarkand State Medical University
Mustafoev O.M.[2]	Public health technikum named after Siyab Abu Ali ibn Sino[2] Samarkand, Uzbekistan

ABSTRACT

To date, a number of techniques and anti-spay coatings have been developed and successfully used in experimental studies. Their role is to activate fibrinolysis, impede coagulation, reduce the inflammatory response, inhibit collagen synthesis or create a barrier between adjacent wound surfaces[1]. It is well known that some basic surgical principles should be followed in all abdominal surgeries. Damage to the peritoneum should be avoided by careful tissue handling, careful hemostasis, continuous irrigation and avoiding unnecessary drying, ineffective use of foreign bodies and suturing or tissue clamping [2].

Keywords: efficacy evaluation, antispaque coating, wound model, lung, experiment

Introduction: The use of thin and biocompatible suture materials, atraumatic instruments and starch-free gloves is also recommended. In addition, liquid and solid mechanical barriers have now been developed to prevent the formation of postoperative peritoneal adhesions between damaged serosal surfaces during the 5-7 days required for re-epithelialization of the peritoneum [3]. An ideal anti-adhesion coating should be biodegradable, non-inflammatory, non-immunogenic, persist during the critical phase of re-epithelialization, remain in place without sutures or staples, remain active in the presence of blood and be quick and easy to apply, in addition, it should not interfere with healing, promote infection or cause adhesions [4]. Anti adhesion coatings are currently considered to be the most useful adjuncts that can reduce the formation of postoperative peritoneal adhesions.

There are non-absorbable and bioabsorbable films, gels or solid antispaque membranes. The most commonly used mechanical barriers are oxidized regenerated cellulose, expanded polytetrafluoroethylene, hyaluronic acid-carboxymethylcellulose and polyethylene glycol [6]. The most widely studied bioabsorbable films are Seprafilm and Interceed. Seprafilm is absorbed within 7 days and excreted within 28 days. Prospective randomized controlled trials have shown the efficacy of Seprafilm in reducing the incidence and extent of postoperative adhesions [7]. However, Seprafilm can cause significant disruption of anastomoses and should not be used in cases where they are overlapped. Other experimental studies have shown that covering parietal peritoneal lesions with microsurgical autologous peritoneal grafts can completely prevent the formation of severe peritoneal adhesions [8] However, the advantage of a synthetic barrier is that the material does not need to be surgically obtained and can be cut to size outside the abdominal cavity and then sutured without sutures [9]. Thus, a number of studies have been conducted on the prevention of adhesions, but the results are encouraging, but most of them are controversial and have been conducted on experimental models.

Purpose of the study: Evaluation of the effectiveness of the antispaic coating on the lung wound model in the experiment

Materials and methods of research. Experiments of lung wound formation with subsequent evaluation of the effectiveness of antispaecal coating from cellulose derivatives were carried out on the basis of GU "RSNPMCH named after Acad. V. Vakhidov", Department of Experimental Surgery in 2019. White mongrel rats in the number of 32 animals were used as experimental animals. A total of 2 series of experiments control and experimental groups were performed. Anesthesia was performed using an anesthesia machine RO-6 with oxygen supply. The mode of ventilation was carried out with a frequency of 24 per minute and a volume of up to 30ml. For mask anesthesia a special rubber nozzle was used, which was put on the animal's face and covered hermetically the area of head-neck transition. The volume of the mask is 50ml. The mask has a check valve for exhalation of air.

Surgical technique. Skin and superficial muscle incision in the area of the 6th intercostal space up to 3 cm long. The pectoral muscles were laxed along the course of the muscles (Fig. 1)

Figure 1. Skin incision in the area of the right side of the thorax

In the 6th intercostal region, thoracotomy was performed using an instrument - mosquito type blunt instrument (Figure 2).

Figure 2. Dilation of the pectoralis muscle, isolation of the intercostal space

The wound was dilated to 1.5 cm and then hooks were inserted to widen the wound (Fig. 3).

Figure 3. Use of Mosquito-type clamp for opening and pleural cavity and dilatation of the intercostal space

The right lung is moderately collapsed, breathing during mask anesthesia, air. Using atraumatic microclamps, the right lung was withdrawn into the thoracotomy wound. The anterior surface of the lung was injured using a bipolar coagulator (Figure 4).

Figure 4. Application of the lesion to the lung using a bipolar coagulator

On a surface of 1cm2 5 lesions each measuring up to 2mm in diameter. No air bubbles were observed during the test with the injection of physiological solution.

Figure 5. Application of antispaque coating on the wound surface of the lung

In the control group of animals, the lung was plunged back into the right pleural cavity. Further, a microcatheter was left and the thoracotomy wound was sutured hermetically at first by suturing the edges of the chest muscles followed by the skin wound. After achieving hermeticism, air from the pleural cavity was suctioned through the catheter and the catheter was removed. Lung ventilation was performed with oxygen until the animal was fully awakened. Next, the rat was moved to a separate cage for observation. During 3 days water with addition of ipobrufen at the rate of 0.5 g per 100ml of water was given.

In the experimental group of animals, a special anti-spay coating made of cellulose derivatives was applied to the area of lung injury (Fig. 5)

At the present period lung surgery is more oriented not on prevention of adhesions, but on their formation, in particular, to prevent the development of recurrent pneumothorax, etc. However, the purpose of this part of the experimental and morphological study was to additionally confirm the effectiveness of hemostatic coating Heprocel in terms of preventing the development of postoperative adhesions. By analogy with the previous experiment, 32 white mongrel rats were used as experimental animals. In total, 2 series of experiments were performed in control (17 animals) and experimental (15 animals) groups. After adhesion and uniform distribution of the coating on the lung surface, the next stage was carried out. To prevent the process of cellular inflammation, blood serum was applied to the adhesive coating using a syringe (Figure 6). As a result, within 1-3 minutes, the coating turned into a translucent film of soft-elastic consistency, did not prevent the lung from stretching during breathing, and adhered tightly to the wound surface (Fig. 7).

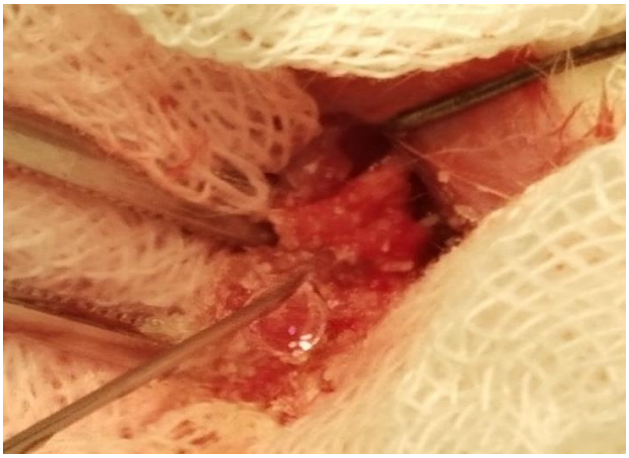

Figure 6. Application of blood serum on powder coating to form a translucent film on the wound surface.

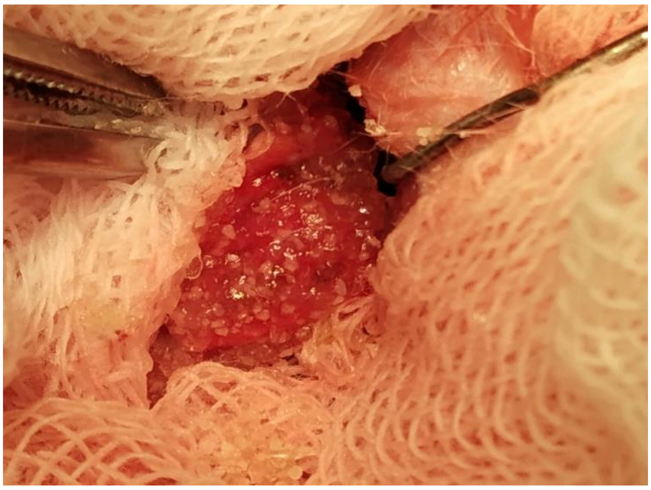

Figure 7. Formed coating on the surface of the lung wound.

When the coating is formed using blood, it takes on the character of a thrombus, which promotes the formation of a denser coating followed by cellular inflammation-type biodegradation as the thrombotic masses resorb (Figure 8).

Figure 8. Coating pattern when using blood to form hemostatic coating using Heprocel implant.

A similar coating was also formed on the wound surface of the parietal pleura, where access to the pleural cavity was made. Then the operation was completed as in the control group.

During the experiments, lethal outcome was observed in 2 cases. In the first case in the control group, lethal outcome occurred due to respiratory depression in the early postanesthesia period. In the second case in the early postoperative period lethality occurred as a result of lung collapse in the control group.

In the control group.

1 day. After the performed operations on the first day, all other operated animals were alive, active, took food and drank water (with the addition of ipobrufen for anesthesia). No phenomena of crepitation and pathologic mobility of the thorax were observed in the area of the postoperative wound. Sutures lay well, there were no signs of inflammation. The right and left halves of the thorax are actively involved in breathing.

3 day. The animals are active, moving around the cage. They drink water well and take feed. There are no signs of inflammation in the area of the surgical wound. The thorax is evenly involved in the act of breathing. No painful sensations in the area of the postoperative wound were noted when taking the animals on hands.

7 day.The condition of the operated animals without special pathological changes. The postoperative wound healed in both groups of rats. At palpation both halves of the thorax and the wound area are painless. The weight of animals changed insignificantly, the difference in both groups of animals is not statistically significant (Table 1).

14 day. The condition of animals is good. They are active. They take food and drink water. The postoperative wound has healed. Sutures from the wound are removed, there is no discharge. Palpation of the wound area painless. Breathing is carried out. Pulse is within normal limits.

During the observation of the operated 17 animals in the control group signs of wound suppuration were noted in 2 cases. The average period of complete wound healing amounted to 6 days.

The main group of animals.

In the main group of 15 animals in the postoperative period, care and anesthesia were carried out similarly to the control group. No significant changes in behavior, physiological and general condition were observed. Complications in the form of superficial wound suppuration were noted in 1 rat, which was stopped after removal of the skin thread. The period of wound healing averaged 5-6 days

Dynamics of animal weight indices are presented in Table 1.

Data of macroscopic studies.

As planned, on the 7th day after the operation 5 rats from each group were taken out of the experiment to evaluate the condition in the pleural cavity after modeling the lung wound (2 animals in the control group died in the early postoperative period).

Table 1.
Dynamics of animal weight after exposure

Group	Prior to exposure	7 day	14 day	21 day
Control	176 ± 12	150 ± 13	160 ± 14	175 ± 12
Experimental	174 ± 14	165 ± 15	171 ± 15	178 ± 14
t-criterion	0,43 P>0,05	1,69 P>0,05	1,20 P>0,05	0,36 P>0,05

In the control group on the 7th day. At autopsy of the thorax after euthanasia according to the provisions on humane treatment of animals, it was revealed: the left pleural cavity was intact, the lungs after air intake were collapsed, airy. The pleural cavity is clean. No adhesions and pathologic manifestations were revealed. The right pleural cavity (from the side of the performed operation), without pathologic effusion. There are massive fusions between the lungs and parietal pleura. The area of surgical access in the 6th intercostal space is also in adhesions with the right lung (Fig. 9).

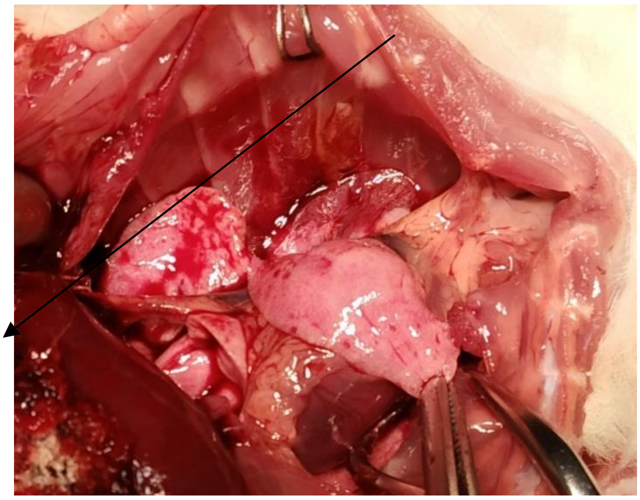

Figure 8. 7 day control. Planar adhesion of the lower lobe of the right lung with the parietal pleura in the area of thoracotomy wound.

The adhesions are separated from the lung by blunt exploration, in some places the visceral pleura is torn. Counting the number of specks revealed that in 5 points of the defect, adhesions with the parietal pleura were formed in most cases. In the wound area, adhesions occurred along the entire course of the surgical access. Of the 5 rats studied, all cases had adhesions, which were in most cases planar in nature. The area of soft tissues of the thorax and skin had no signs of infection, there was no discharge.

In the main group on the 7th day also 5 animals were taken out of the experiment. As in the control group in the left pleural cavity no pathologic changes were revealed. At autopsy of the right pleural cavity there is a loose adhesive process in the area of point defects in the region of the anterior surface of the lung. Of the 5 animals examined, 2 had 3 adhesions out of 5 lesions and one had a single adhesion out of 5 lesions. Visually there was no evidence of the presence of a coating, the visceral surface of the lung was covered with a thin shiny film without color. The adhesions are easily detached without damage to the visceral pleura. The lung is airy, not deformed. In the area of the surgical wound in the 6th intercostal space there are also flat loose adhesions in all cases out of 5, easily separated.On the 14th day after the operation in the control group the chest autopsy revealed the following: the left pleural cavity was intact, the lungs after air intake were collapsed, airy. The pleural cavity is clean. No adhesions and pathologic manifestations were revealed. The postoperative wound in the area of the right half of the thorax is clean, without infiltration. Only in 1 case there was soft tissue suppuration with abscess formation in the ligature area. Right pleural cavity without pathologic effusion. There are adhesions between the lungs and the parietal pleura (Fig. 9).

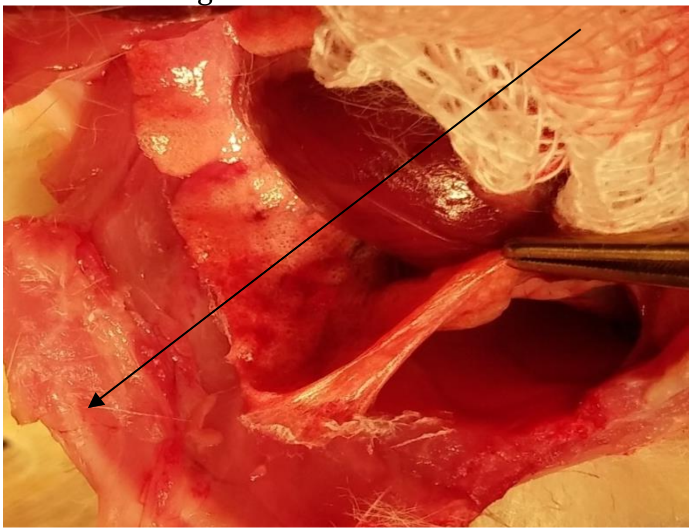

Figure 9. 14 days. Adhesions between visceral and parietal pleura in the form of ties in the control group

The area of surgical access in the 6th intercostal space is also in adhesions with the right lung. The adhesions are poorly separated from the lung by blunt dilatation, a tear of the visceral pleura is noted. Counting the number of specks is difficult due to the confluence of the adhesions. The majority of adhesions are presented in the form of ties in 2 cases due to the planar adhesion of visceral and parietal pleura (Fig. 10). In the area of the previously performed thoracotomy wound, adhesions with the visceral pleura were in the form of thin thighs.

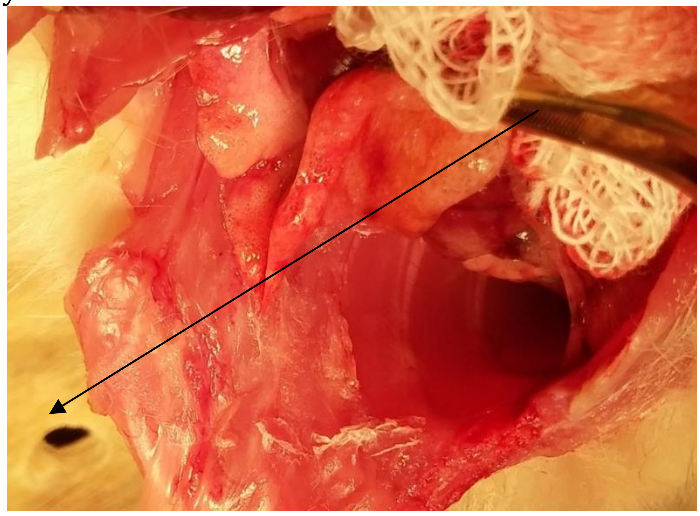

Figure 10. 14 days. Planar adhesions between visceral and parietal pleura in the control group.

In the main group, 5 animals were also withdrawn from the experiment on the 14th day. As in the control group, no pathologic changes were revealed in the left pleural cavity. At autopsy of the right pleural cavity there was a single adhesion in the area of point defects in the region of the anterior surface of the lung. Of the 5 animals examined, adhesions were detected only in 1 animal in other cases no adhesions were revealed. In the area of the previously performed thoractomy wound no adhesions were detected in any case (Fig. 11).

The area of lung injury is defined by barely visible scars and thickening of lung tissue. Lung excursion is not disturbed. Visually there are no signs of the presence of the coating. In the area of soft tissues where thoracotomy was performed, no inflammatory process was detecte

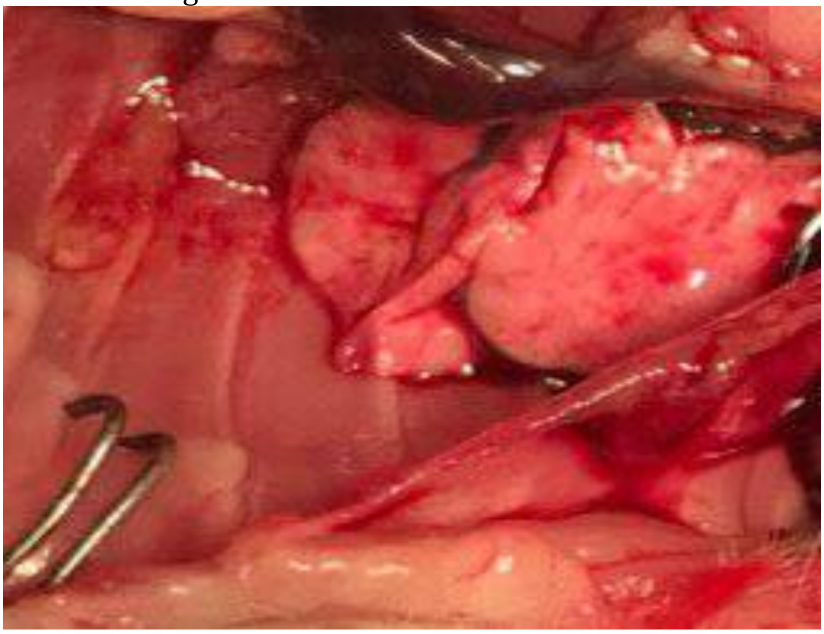

Figure 11. 14 days. Absence of lung adhesions in the experimental group of operated animals

On the 21st day after surgery. Chest autopsy in the control group revealed the following: the left pleural cavity was intact, the lungs were collapsed, airy after air intake. The pleural cavity was clean. No adhesions and pathologic manifestations were revealed. At autopsy of the right pleural cavity there is no pathologic effusion. There are adhesions between the lungs and the parietal pleura in the form of ties (Fig. 12).

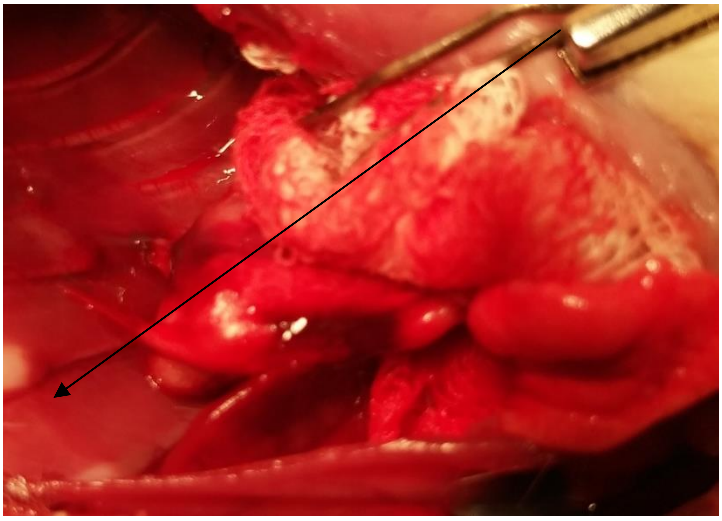

Figure 12. Control 21 days. There is an adhesion process between visceral and parietal pleura in the form of dense ties and planar adhesions.

In the area of surgical access in the 6th intercostal space, adhesions in the form of thin ties to the right lung were also detected. The adhesions separated from the lung with formation of visceral pleura tears. Of the 5 rats studied, all cases had adhesions. The area of soft tissues of the thorax and skin had no signs of infection, there was no detachment.

In the main group on 21 days 5 animals were taken out of the experiment. No pathologic changes were revealed in the left pleural cavity. At autopsy of the right pleural cavity the lungs collapsed, no signs of formed adhesions between visceral and parietal pleura were revealed. Only in 1 case there was a thin cord between the area of the surgical wound and visceral pleura (Fig. 13). The surgical wound was completely healed, there was no infiltration, tissue layers were distinguishable.

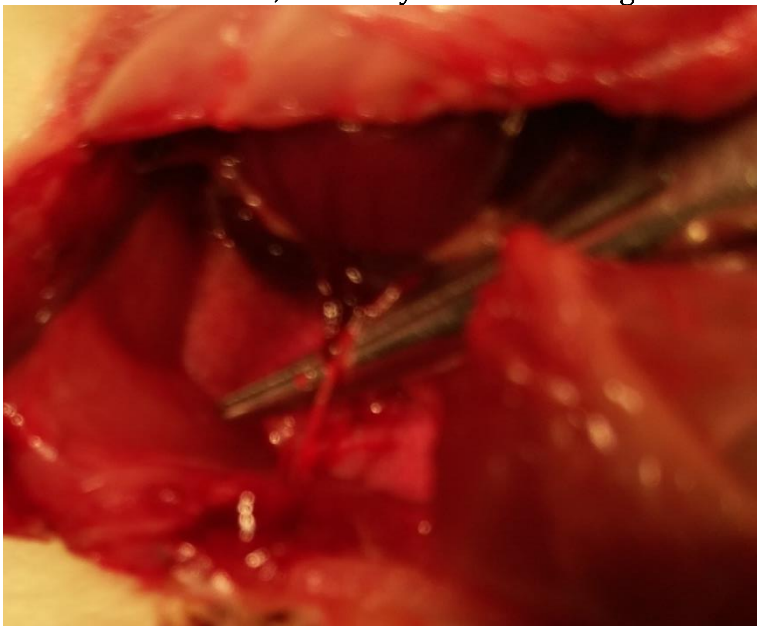

Fig. 13: Thin traction between the parietal and visceral pleura in the area of the postoperative wound in the main group

In this study, it was possible to demonstrate that the use of an antiadhesion coating reduced the risk of adhesions and the nature of their development (flat or in the form of thrusts) (Table 2; Fig. 14).

Thus, the objective of the experimental studies was to create a model of lung injury that would allow inducing adhesions in the pleural cavity while not causing complications such as pneumothorax, pleurisy, and pleural empyema. The model should be feasible and reproducible while avoiding severe complications and fatalities. The second task was to evaluate the effectiveness of hemostatic domestic implant Heprocel in preventing the formation of adhesions in the pleural cavity by a new method of elastic coating formation using blood serum instead of blood. Thus the formed coating does not have the character of a thrombus, i.e. it does not contain erythrocytes, in this connection it allows to prevent the presence of blood cell elements in the process of biodegradation, thus preventing the formation of adhesions.

The model of lung injury in the form of right-sided thoracotomy with minimal tissue bleeding due to blunt separation of soft tissues and intercostal muscles allowed to exclude the use of physical and chemical methods of hemostasis. Damage of a certain surface of the right lung allowed to form a standardized model of lung injury. In this case, the left pleural cavity served as a control. The operations were performed by original mask anesthesia using halothane vapor with oxygen in a special vaporizer.

The postoperative period proceeded without complications. The study of animal condition, physiologic parameters, as well as macroscopic changes during withdrawal of animals from the experiment allowed us to come to the following conclusion. The domestic hemostatic implant Heprocel adheres well to the tissues of the damaged lung, as well as to the edges of the surgical wound. The use of blood serum allows to achieve the formation of soft-elastic coating on the surface of the lung wound, which does not deform the lung and stretches during lung excursion. In comparison with the control group of animals the new coating almost completely prevents the expressed adhesion process in the pleural cavity, thus preserving physiologic lung excursion after wound exposure. The process of biodegradation is not accompanied by inflammatory reaction of tissues and effusion in the pleural cavity. Wound healing occurs in usual terms. Behavior of animals and their condition do not undergo significant changes. Weight gain of animals begins already in 14 days after the operation.

Conclusions: Thus, the new method of coating formation using the domestic implant Heprocel can be applied after performing surgical interventions on the lungs in order to restore the physiological parameters of respiration in the most complete way.

List of references used:

1. Воробьев А.А., Калашников А.В., Салимов Д.Ш. Патологические проявления внутриплевральной адгезии. Современнная наука и инновации. 2017;1:183-189.
2. Kouritas VK, Kefaloyannis E, Tcherveniakov P, et al. Do pleural adhesions influence the outcome of patients undergoing major lung resection? Interact Cardiovasc Thorac Surg. 2017;25(4):613-619.
3. Калашников А.В., Дворецкая Ю.А. Сравнительный морфологический анализ внутрибрюшинных и межплевральных сращений. Журнал анатомии и гистопатологии. 2016;51:26-31.
4. Tamura M, Matsumoto I, Saito D, et al. Dynamic chest radiography: Novel and less-invasive imaging approach for preoperative assessments of pleural invasion and adhesion. Radiol Case Rep. 2020;15(6):702-704. Published 2020 Apr 6. doi:10.1016/j.radcr.2020.02.019
5. Baxter J, Lima TA, Huneke R, et al. The efficacy of hydrogel foams in talc Pleurodesis. J Cardiothorac Surg. 2020;15(1):58. Published 2020 Apr 15. doi:10.1186/s13019-020-01098-y
6. Gumán-Valdivia-Gómez G, Tena-Betancourt E, de Alva-Coria PM. Postoperative abdominal adhesions: pathogenesis and current preventive techniques. Adherencias abdominales postoperatorias: patogénesis y técnicas actuales de prevención. Cir Cir. 2019;87(6):698-703. doi:10.24875/CIRU.18000511
7. Yasukawa M, Taiji R, Marugami N, et al. Preoperative Detection of Pleural Adhesions Using Ultrasonography for Ipsilateral Secondary Thoracic Surgery Patients. Anticancer Res. 2019;39(8):4249-4252.
8. Aysan E, Sahin F, Catal R, Javadov M, Cumbul A. Effects of Glycerol and Sodium Pentaborate Formulation on Prevention of Postoperative Peritoneal Adhesion Formation. Obstet Gynecol Int. 2020;2020:3679585.
9. Калашников А.В., Дворецкая Ю.А. Сравнительный морфологический анализ внутрибрюшинных и межплевральных сращений. Журнал анатомии и гистопатологии. 2016;51:26-31.
10.Eshonxodjaev O.Dj., Dusiyarov M.M., Xujabaev S.T., Sherkulov K.U., Radjabov J.P. The Main Directions Of Prevention Of Adhesions In Abdominal And Thoracic Surgery. European Journal of Molecular & Clinical Medicine .ISSN 2515-8260 Volume 07, Issue 03, 2020. 5214-5222
11.Eshonxodjaev O.Dj., Dusiyarov M.M., Xujabaev S.T., **Rustamov I.M.** Estimation of the efficiency of antisseal coating on the model of lung wound in experiment. Central asian journal of medical and naturals ciencesVolume: 01 Issue: 04 | Nov-Dec 2020 ISSN: 2660-4159. 1-6.
12.Eshonxodjaev O.Dj., Dusiyarov M.M., Xujabaev S.T., **Sherbekov U.A., Sherkulov K.U.** The main directions of prevention of adhesions in abdominal and thoracic surgery. Academicia an International Multidisciplinary Research Journal DOI: 10.5958/2249-7137.2021.01141.1Vol.11. 906-915.