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STUDY OF THE BIOLOGICAL COMPATIBILITY OF PN-90 POLYTETRAFLUOROETHYLENE ON EXPERIMENTAL ANIMALS

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Polymer products are widely used in the field of medicine in the form of implants, artificial vessels, heart valves, etc. However, the tasks of searching, developing and studying the properties of polymeric materials for medical purposes remain relevant. This paper presents the results of biocompatibility research of PN-90 polytetrafluoroethylene implanted in the subcutaneous fat space of laboratory animals (Wistar rats). The implantation of the polymer was carried out under general anesthesia in the subscapular area. Histological sections of tissues from the control area and adjacent to the implant were studied. Around the implanted polytetrafluoroethylene there was is an intensive growth of new vessels of various calibers combined with severe fibroblasts proliferation. The polymeric material was also investigated by means of an IR spectrometer and a scanning electron before and after implantation. According to the results of IR spectroscopy the chemical composition of the polymer remained unchanged. The surface of polytetrafluoroethylene after implantation was practically identical to the surface of the initial polymer. Based on the data obtained, it can be concluded that polytetrafluoroethylene is biologically compatible and can be used in medicine as a base for implants.

Keywords: biocompatibility, inflammation, wear resistance, implantation, polytetrafluoroethylene, rats.

Introduction. Synthetic polymer materials are widely used in medicine as consumables, drug delivery systems, prostheses and implants, extracorporeal devices, etc. In most cases, the use of polymers is caused by the cheapness and manufacturability in the production process as well as the ability to easily vary their operational properties. Also, a number of requirements are presented to the materials implanted into the human body including: high biocompatibility, chemical inertness, high purity of the product, wear resistance, stability of the main characteristics [1].

A polymer suitable for use in medicine is polytetrafluoroethylene (PTFE) or Teflon. It is a waxy and smooth synthetic polymer material widely used in industries and medicine. It has very high thermal and chemical stability, low coefficient of friction and high hydrophobicity. The list of its properties includes: biocompatibility, corrosion resistance, inertness and relatively low cost. The first medical use of PTFE was in making of artificial heart valves. Subsequently, the scope of application gradually expanded with the development of vascular grafts, supports for bone regeneration and prostheses for hernia repair [2-7].

The degree of biological compatibility of materials is studied on laboratory animals by surgical implantation into physiological spaces. Compatibility is determined by the immunogenicity and the nature of inflammatory processes in the tissues of the body around the study object. During the implantation of materials tissue changes are most pronounced with minimal traumatic effects of a foreign object. Most often, the implantation of the samples is carried out in the hypodermic or subcutaneous layers. Evaluation of the reaction of surrounding tissues to implantation is performed by comparing morphological signs of inflammation, migration of immunocompetent cells and vascularization in the tissues around the implanted material with morphological characteristics of tissues from intact areas of symmetrical zones using microscopy. The absence of a local pathogenic effect is determined indirectly with the use of subcutaneous implantation tests. Taking into account the size of the implanted materials and the short duration of the experiment, small rodents and rabbits are used as test laboratory models [8-9].

The purpose of this study is to test the biocompatibility of PN-90 grade PTFE in vivo on laboratory animals.

Materials and Methods. PN-90 brand PTFE (GaloPolymer, Russia) was used as the implantable material with an average particle size of 90 μm and 2.16 g/cm^3 density. PTFE samples were obtained by cold pressing in a PKMV-100 hydraulic press (Impuls, Russia). The pressing was conducted at room temperature with 50 MPa pressure and further sintering in a SNOL 15/900 (Umega Group, Lithuania) programmable furnace at 375 °C.

The study of wear resistance was evaluated on a UMT-3 tribological machine (CETR, USA) with "finger-disc" friction scheme according to GOST 11629-2017. During the test, the change in volume (ΔV, cm^3), the rate of mass wear (I, mg/h) and the coefficient of friction (f) of the material were determined.

IR spectra of implanted PTFE before and after surgery were obtained on a Varian 7000 FT-IR (Varian, USA) Fourier-transform IR spectrometer. The spectra were obtained using attenuated total reflection (ATR) accessory in the range of 500-4000 cm^{-1}.

Using a scanning electron microscope (SEM) JSM-7800F (Jeol, Japan) in the secondary electrons mode at low accelerating voltage the supramolecular structure of the material was studied before and after implantation.

In vivo study was conducted on the 3 laboratory rats (Wistar line) at the age of 4 months, weighing 450-500 grams. For the operation the laboratory rats were put into general anesthesia by intramuscular injection of 2% xylazine solution at the rate of 0.05 ml per kg of animal body weight and a "Telazol 100 mg" solution containing 50% tiletamine and 50% zolazepam at the rate of 40 ml of the drug per 100 grams of animal body weight. A longitudinal incision was made parallel to the spine line through the entire thickness of the skin with a length of 0.5-0.8 cm then 2 cm long channel with a blind thickening towards the iliac region was formed with a scalpel to contain the implant (Fig. 1) fixed by natural connective tissue formations. Hemostasis was carried out with a sterile cotton swab. The implants measuring 0.5x1.0 cm in width and length were inserted into the formed pocket. Implant fixation was controlled visually and by palpation. The wound was sewn up with a simple continuous interrupted suture.

After 10 days the implant was extracted with a biopsy of all tissue layers in one block directly above the implant. The biopsy area was determined by palpation. Tissue layers were biopsied from the opposite side of the dorsal region for control comparison. The tissues adjacent to the implant were examined visually after removal. All biopsies were placed in a 10% solution of neutral formalin and provided to the histological laboratory for preparation of specimens. Biopsies were enclosed in paraffin wax at an EG 1150 (Leica Microsystems, Germany) histological station. Histological sections with a thickness of 3-5 μm were made on a SM2010R (Leica Microsystems, Germany) semi-automatic sledge microtome. The samples were stained with hematoxylin and eosin on a Autostainer XL (Leica Microsystems, Germany) instrument and sent for examination using an optical microscope.

The study of histological tissues sections after implantation of polymer materials into a laboratory animal was carried out using an BX-41 (Olympus, Japan) optical microscope.

Results and Discussion. The results of tribological studies of the polymer material are presented in Table.

The initial PTFE has average wear resistance values but these characteristics can be varied up to the required properties by adding fillers to the polymer. The nature of the fillers is determined depending on the purpose of the final material [10-11].

The IR spectra of the PTFE implant before and after the clinical trial are shown in Fig. 2.

The peaks showing the most intense absorption bands have 1200 and 1146 cm^{-1} wave numbers and belong to the stretching vibrations of the -CF_2- groups. Oscillations at 640 cm^{-1} are attributed to the wagging vibrations of γω(-CF_2-) and bands at 555 cm^{-1} correspond to deformation vibrations of -CF_2- groups. Also, according to the IR spectra, the material before and after implantation retained its original properties. Thus, it was not subjected to any changes in the body of the laboratory animal [12].

Changes in the morphology of the PTFE surface before and after implantation surgery were investigated by SEM (Fig. 3).

After implantation, the surface of the material did not undergo significant changes (Fig. 3, b) compared to the initial one (Fig. 3, a). Some microprotrusions were formed after implantation which probably appeared after cyclic loads on the polymer occurring in a living organism. To exclude further changes, it is possible to modify the physical and mechanical properties of polymer samples based on PTFE by various methods. It will increase the range of applications of the material in implantology.

Figure 4 shows histological sections of tissues from the control zones and from the area around the implant.

A comparative characterization of histological tissue samples was implemented from unaffected areas as control samples (Fig. 4, a) and around implants (Fig. 4, b). On the 10th day of inflammation, the proliferative stage of inflammation and the final stages of exudation began. The stage was characterized by the active growth of cells involved in the repair processes and the growth of new vessels. The presence of edema and neoangiogenesis indicate the intensity and duration of the exudation stage. The degree of immunoreactivity for the presence of foreign material was assessed by the number of migrated lymphocytes and macrophages. The inflammatory infiltrate in all samples was partially filled with fibroblast-like cells which indicates the activation of reparative processes [13].

Fig. 1. A laboratory rat during PTFE implantation

Results of tribological studies

Characteristics	ΔV, см^3	I, мг/ч	f
PN-90 PTFE	0.07	51.39	0.23

Note: ΔV – volume change, cm3; I – mass wear rate, mg/h; f – coefficient of friction

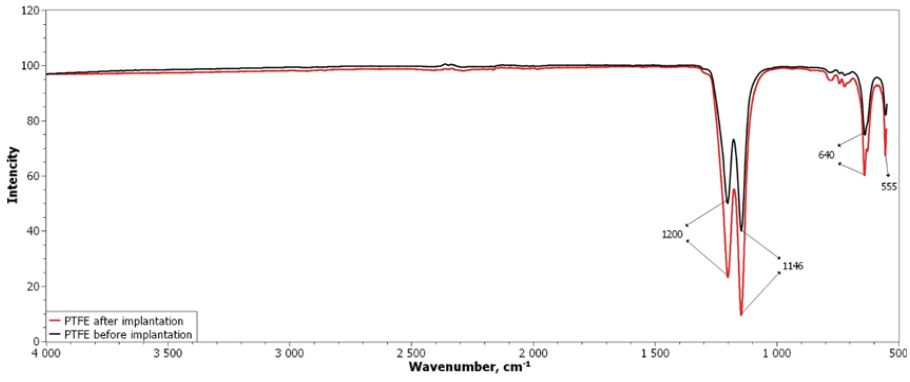

Fig. 2. The IR spectra of the PTFE implant

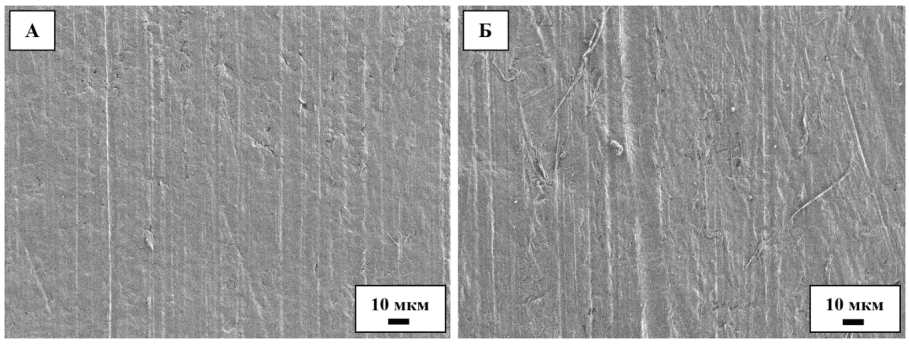

Fig. 3. SEM images of the PTFE surface before implantation (a) and after implantation (b)

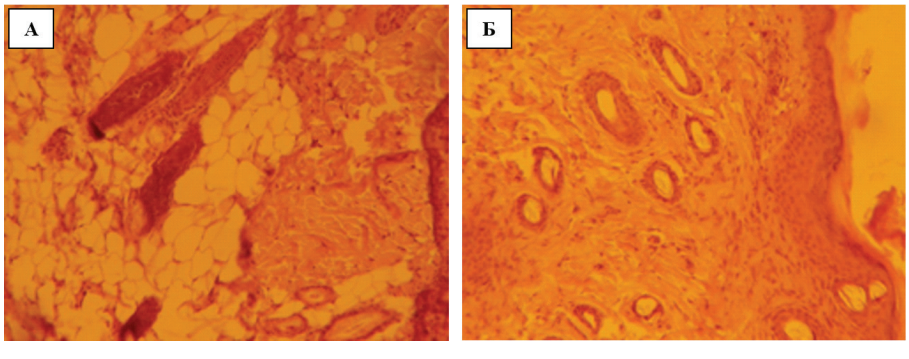

Fig. 4. Histological sections of rat tissues: the control area (a) and the area around the PTFE implant (b)

Intensive growth of new vessels of different calibers is observed around the implanted polymer in combination with a strong proliferation of fibroblasts in all layers of the dermis. This may indicate the onset of a proliferative stage of inflammation and the beginning of reparative processes. The number of fibroblast-like cells in the field of vision varies from 50 to 80 cells. However, there is a low infiltration of immunocompetent cells – the number of mononuclears in the field of vision is on average 20 ± 5 cells. This indicates a low degree of immunoreactivity and destructive processes.

Conclusion. The conclusions based on the results of studies of the biocompatibility of implanted PTFE in the laboratory animal:

- by IR spectroscopy it was found that the PTFE implant did not undergo chemical changes in the body of the laboratory animal;
- SEM results revealed that the polymer surface did not undergo significant changes in the body of the laboratory animal;
- biological PTFE inertness was observed in histological sections, it was manifested by the almost complete absence of an immune response from the body and the polymer easily germinated into the surrounding tissues of the body and was securely fixed by the communicating system of voids.

The results obtained indicate chemical resistance, low toxicity and immunogenicity in vivo. This determines the relevance of the practical application of PN-90 PTFE in medicine as a biologically compatible material. In the future, it is planned to conduct more extensive and long-term preclinical tests for biological compatibility.

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THE RELATIONSHIP OF HYPERURICEMIA WITH ARTERIAL HYPERTENSION AND RISK FACTORS FOR CARDIOVASCULAR DISEASES IN THE WORKING POPULATION OF SOUTHERN YAKUTIA

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A one-stage population study was conducted in the working population in south Yakutia. The 174 people of non-indigenous nationality were examined. Increased uric acid (UA) levels were found in 27% of the individuals. The association of UA level with BMI, OT, lipid spectrum was revealed mainly in men, systolic blood pressure and blood glucose in women. Abdominal obesity was equally frequently recorded in both men and women, regardless of the presence or absence of hyperuricemia, Logistic regression showed satisfactory information content of the prognostic significance of the level of UA with hypertension only in the female population. Hyperuricemia was not an independent risk factor for the development of cardiovascular pathology.

Keywords: uric acid, hypertension, obesity, lipid spectrum, non-indigenous population, south Yakutia.

Arterial hypertension (AH) remains one of the most common diseases of the cardiovascular system, becoming epidemic in nature. Correction of risk factors, along with decreasing blood pressure, affect the prevention of cardiovascular complications. Over a 20-year period, the prevalence of hypertension in Russia increased from 39.2% to 45.7% [1].

In recent years, there has been a trend towards an increase in hyperuricemia (HU) among the world's population [8]. Multicenter studies by URRAH and NHANES have shown that asymptomatic HU is associated with the development of hypertension, coronary heart disease, obesity, diabetes mellitus, etc. [8,16]. Foreign authors have proven the influence of HU on the prognosis of cardiovascular complications as well [10,12,14]. A retrospective cohort study of 5899 people demonstrated that an increase in UA levels is a powerful factor in the transformation of prehypertension into hypertension [12], and also increases the risk of developing metabolic syndrome, dyslipidemia, diabetes and CKD [14]. Certain data is based on the fact that HU activates the renin-angiotensin system (RAS) and blocking RAS inhibits the action of xanthine oxidase [15]. Nevertheless, a possible direct connection of HU with the development of hypertension is still being discussed.

The aim of the study was to identify the relationship of hyperuricemia with arterial hypertension and its risk factors in the working population of non-indigenous nationality in Southern Yakutia.

Materials and methods of research. A single-stage study of the working population of the Republic of Sakha (Yakutia) of the Aldan district according to the list of industrial businesses was conducted within the framework of research on the State assignment of the YSC CMP "Normal and pathological regional peculiarities of biochemical, immunological and morphological indicators in the indigenous and alien population of the Republic of Sakha (Yakutia)" (FGWU-2022-0014) with a response rate of 75%. 174 people, representatives of non-indigenous nationality (Russians, Ukrainians, etc.) arrived for the examination. The median age was 44 [36; 52] years. 108 women, and 66 men were examined. They were comparable in age for analysis. The main condition for inclusion in the study was the absence of gout, subcutaneous tofuses.

All respondents underwent a questionnaire, an anthropometric study measuring height, body weight, waist circumference (WC) and hips circumference (HC), and blood pressure (BP) measurement. For laboratory tests, venous blood was taken on an empty stomach in the morning 12 hours after the last meal. All par-

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