

**PROGRESS OF THE REGENERATIVE PROCESSES  
IN ARTIFICIAL SKIN WOUNDS AGAINST  
THE BACKGROUND OF A PRELIMINARY CHRONICAL  
INTOXICATION WITH PHOSPHOR-ORGANIC  
PESTICIDE "ZOLON"**

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The posttraumatic regeneration of the skin is a complex process and its course (progress) can be accelerated or delayed under the influence of various factors of the organism itself and the environment. In the available literature there are many data of stimulative or depressive effect on the progress of the skin regenerative processes. For example: Some hormones (5,20), ascorbic acid (18), medicines — (1,19) etc. influence on the processes. On the other hand, very scarce facts can be found about the effect of the production-environment (4, 16).

The investigation of the posttraumatic skin regeneration of agricultural workers arouse certain interest: they contact constantly some chemicals and their work itself suggests more often wounds and injuries. It is already known that pesticides have a depressive effect on the immunological reactions (1, 13, 21), also that after certain disorders, of the immune mechanisms, the regulation of the regenerative processes is disturbed (3, 15).

Presuming all that, we have for an object of the present study to follow the regenerative skin processes after a preliminary intoxication with phosphororganic pesticide "Zolon" (PPZ) applied as a plant-protector in agriculture.

**Material and methods**

The study covers 63 white male rats with initial weight of 120—140 gm, which were given PPZ per os (doses  $1/100$  and  $1/500$  LD<sub>50</sub>) in an aqueous solution for 5 months every day. The animals were divided in groups of 7. 21 of them were control. After the 5<sup>th</sup> month subcutaneous tissue wounds were performed under an ether narcosis. The dimentions of the wounds were 2/2 cm. Each 7<sup>th</sup>, 14<sup>th</sup> and 30<sup>th</sup> day a histological material was taken, fixed in formaline and Carnua-solution. The paraffin cuts (sections) were stained with hemalaun-eosin after the method of van Gieson for the connective tissue. PAS-reaction of Mc Mannus was done to detect the glycogen and Bra-cheau-reaction to establish RNA.

**Results and discussion**

We analyse both doses and their effect on the regeneration of the wounds, because the results of our histological study show a degree difference only, concerning the way and time of the processes.

**Seventh Day:** Both groups of animals perform their wound-regeneration under the crust. The surface wound layer is abundant in leucocytes, forming abscesses here and there (fig. 1). In comparison with the controls, it is obvious that many leucocytes can be found deeply amidst the granulative tissue of the experimental animals. Proliferation of endothelial and

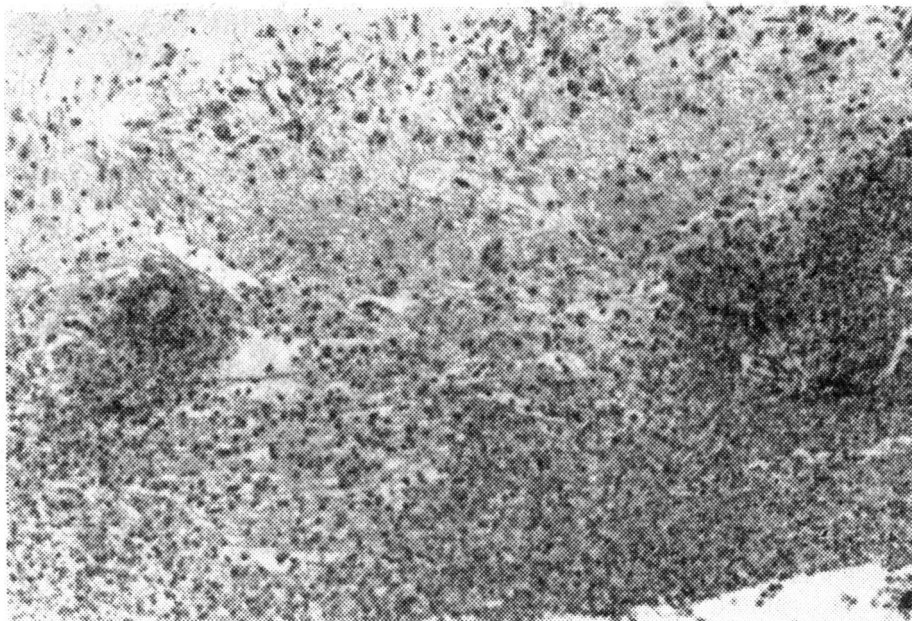


Fig. 1: Abscesses in the superficial vulneral layer of animals treated with  $1/100$  LD<sub>50</sub> PPZ (7<sup>th</sup> day). H.E.,  $M \times 10 \times 10$

adventitic cells is established in "de novo" formed vessels. The granulative tissue of the animals treated with PPZ is loose, swelled, with scarce number of fibroblasts. The cytoplasm of the latter has less glycogen and RNA than that of the controls. The new-formed collagen fibres in the subwound layer are irregularly dispersed and can hardly be stained. The blood vessels in these regions are dilatated and their walls are soaked with PAS (+) nonglycogenic substances. Some wounds of the animals do not produce a granulative tissue, but a heavy swell and leucocyte infiltration is established. The animals treated with  $1/500$  LD<sub>50</sub> PPZ have plasmatic cells together with the grouped leucocytes. The crawling epithelium over the wound is 3 times thicker than normally and the glycogen of the new-formed epithelial cells is irregularly scattered. RNA-quantity is very low. The wound-surrounding tissue of all groups experimental animals is edematic with excess of lymphocytes, plasmocytes, leucocytes and mastocytes; the lymphoid form prevails.

**Fourteenth Day:** Greater number of experimental animals have their wounds covered with detritic materia (not epithelium) with many leucocytes, while the controls show almost final regenerative processes. The granulative tissue is still abundantly irrigated, some blood vessels are dilatated and their walls are soaked with PAS (+) nonglycogenic materia. Increased

quantity of lymphocytes, plasmocytes with pirinofilic cytoplasm and mastocytes is established when compared to the controls. The fibroblasts and fibrocytes are less in number and scarce amount of glycogen and RNA can be detected in their cytoplasm. Near the wound edges new-formed collagenic fibres are found, but greater number of them possess poor tinctorial proper-

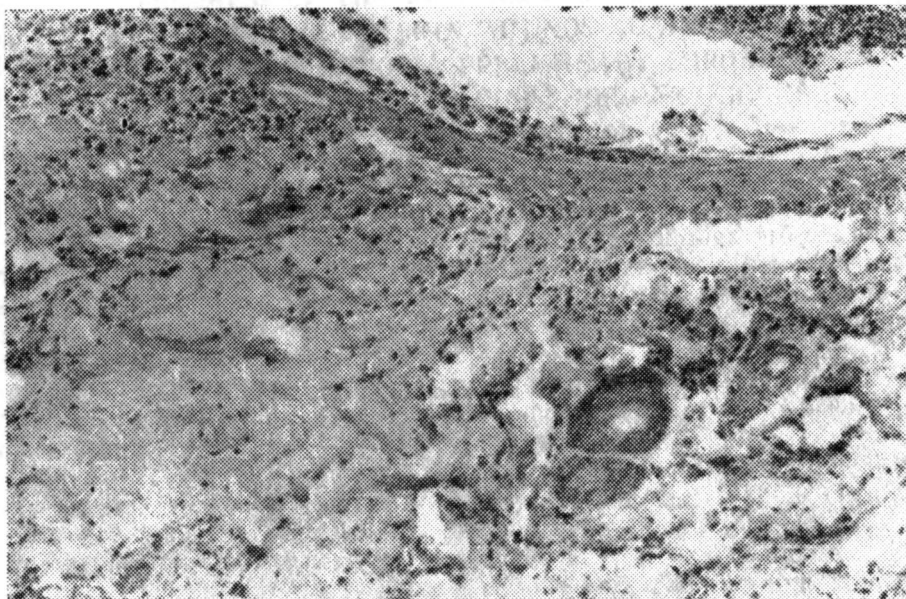


Fig. 2: Thin and infiltrated with leucocytes "crawling" epithelium (14th day). H.E., M.  $\times 10 \times 6.3$

ties. Some of them are quite wrinkled, whirly dispersed, with various thickness. Heaps of PAS (+) structureless materia can be seen amidst the granulative tissue. The surrounding tissue is edematic and possesses round cells mainly. The crawling epithelium over the wound has only 2—3 rows of cells, somewhere is stratificated or infiltrated with leucocytes (fig. 2). It forms deep inserts in the sublocated tissue of some animals. Glycogen can be found only in definite epithelial cells and RNA-quantity does not differ from that of the former group. A cuneiform cicatrice with disorientated collagenic fibres and lymphocytic deep infiltration is established in some of the animals treated with  $1/500$  LD<sub>50</sub> PPZ.

**Thirtieth Day:** Complete epithelization of the wound surface is found in  $2/3$  of the experimental animals, while only one of the controls has an incomplete epithelization. The maturation of the granulative tissue is delayed and unnormal, fields of homogenous cicatrices and hyalinization can be seen. The collagenic fibres are unproperly orientated in greater number of cases. Some of them are rough and undulated. Plasmatic cells, lymphocytes and mastocytes with a lymphoid form can be found amidst the granulative tissue. Leucocyte forming microabscesses are established in the collagenic tissue of some animals. No glycogen is found in the fibroblastotic cyplasma,

but there is certain amount of RNA. Here and there the tissue is edematic and soaked with PAS (+) nonglycogenic substance. The quantity of RNA and glycogen is reduced in the cell-cytoplasma of the covering epithelium. The changes in the animals treated with  $1/500$  LD<sub>50</sub> PPZ are slighter expressed and do not differ considerably from the controls.

Based on the study, it is obvious that animals subjected to a continuous treatment with PPZ could regenerate their skin wounds quite differently concerning the morphological reaction and the terms of production and maturation of the granulative tissue, as well as their epithelization. This is manifested with a suppression of the mesenchymic cell reaction. It is important that there is an excess of leucocytes in the early and later periods, not only in the wound (vulnus) layer, but also in deeper regions. Garshin V. G. (1) suggests that it is an index of the pathological state of the granulative tissue. Besides, the wounds of the control-group animals acquire (since the first days) many fibroblasts with abundant glycogen in their cytoplasma. In comparison with them the wounds of the experimental animals have a slight quantity of this substance, which is extremely important for the regenerative processes (12, 17). To support this fact (wound regeneration — in the way of insufficient granulative tissue) comes the decreased quantity of RNA in the cell elements. Usually, when the wounds recover normally, the RNA-amount in the granulative-tissue cells reaches its maximum about the 8<sup>th</sup>—10<sup>th</sup> day (22), while our investigation of the animals shows that its quantity is still small on the 14<sup>th</sup> day and approaches the control level on the 30<sup>th</sup> day.

Together with the pathology of the granulative tissue, the experimental animals present a suppression of the collagen-production. It is supported by the presence of NMPS in subvulneral tissue until the 30<sup>th</sup> day, presuming that they are necessary to form the collagenic fibres in the early terms of the wound-regeneration (9). The epithelization is also delayed and the crawling epithelium is out of order, thin and infiltrated with leucocytes. Something more: the presence of numerous leucocytes and plasmocytes in the granulative tissue of almost every experimental animal confirms the tension of the cell immunity (1, 14).

The precise mechanism can hardly be explained: the suppression of the wound-regeneration of animals treated with PPZ is unclear. It could be suggested that the active toxic substance tends to a decreased tissue (cell) metabolism, which is a condition of a suppression of the elements of the macrophagial system (10) and regeneration-inhibition. The experiments of Homullo G. V. et al. (11) also prove that the chronic hypoxia tends to an inhibition of the fibrillogenesis and a delay of the regenerative processes. On the other hand the pesticides' action can be direct too: by disorders of the metabolism and a suppression of the oxy-reductive processes (6, 7, 8), resulting in the cell breathing. Undoubtful role play the disorders of the vascular permeability, developed under the influence of the pesticides.

In conclusion, it can be suggested that though slight toxic, the PPZ tends to abnormal course (progress) of the regenerative processes of the wounds. It must be contributed to the hygienic indexes for the workers dealing with this substance.

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**ПРОТЕКАНИЕ РЕГЕНЕРАТОРНЫХ ПРОЦЕССОВ В ИСКУССТВЕННО  
ВЫЗВАННЫХ КОЖНЫХ РАНАХ НА ФОНЕ ПРЕДВАРИТЕЛЬНОЙ  
ХРОНИЧЕСКОЙ ИНТОКСИКАЦИИ ФОСФОРОРГАНИЧЕСКИМ  
ПЕСТИЦИДОМ »ЗОЛОН»**

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РЕЗЮМЕ

Проведено исследование 63 белых мужских крыс, которые затравлялись в течение 5 месяцев фосфорорганическим пестицидом «золон» в дозах 1/100 ЛД<sub>50</sub> и 1/500 ЛД<sub>50</sub>, после чего на спине у животных наносились послынные кожные раны размерами в 2/3 см. Заживление ран прослеживалось на седьмой, четырнадцатый и тридцатый день.

Устанавливается сравнительное замедление регенераторных процессов у животных, которые подвергались действию «золон». Заживление у них отличается от заживления у контролей как созреванием грануляционной ткани, так и ее эпителизацией. Наблюдаются преобладание лейкоцитов в поверхностных и глубоких слоях, подавление мезенхимной клеточной реакции в грануляционной ткани, наличие небольшого количества РНК и гликогена в фибробластах. Сбразующийся над раневой поверхностью эпителий является расселенным, истонченным и инфильтрированным лейкоцитами.

Наблюдаемое замедление регенераторных процессов при заживлении кожных ран объясняется эвентуальной тканевой гипоксией, развивающейся при хронической интоксикации с подавлением пролиферации элементов макрофагальной системы и нарушением процессов заживления, с одной стороны, а с другой — непосредственным токсическим действием пестицида «золон», приводящим к нарушению метаболического обмена и клеточного дыхания.