MORPHOLOGICAL REACTION OF UTERINE WALL TISSUES OF THE WHITE RAT TO A FOREIGN BODY

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At present, the immunity of embryos is receiving considerable attention [2]. Various immunologic reactions (phagocytic, inflammatory, and others) may be of great importance in form-producing processes—in the course of embryonic development and in regeneration phenomena.

Observations [1] on changes in the reactivity of uterine tissues of the mouse in experimentally produced aseptic inflammation show that a great deal remains to be explained about the possible role of inflammatory and phagocytic phenomena in the morphological and physiological rebuilding of uterine tissue.

In the present study we investigated inflammatory and regenerative phenomena in uterine wall tissue of 93 rats in various physiological conditions and at various ages

METHOD

The investigations were carried out on 12-day- and $1^1/_2$-month-old rats, on sexually mature rats in estrus, on pregnant rats (7-14 days), and on rats immediately postpartum.

A foreign body—sterile cotton thread soaked with carmine—was inserted into the wall of the uterus. Insertion of this foreign body, which passed through all the layers of the uterine wall, made it possible to reveal the characteristics of the morphological reactions of its various tissue systems.

The experimental animals were killed at 10 minutes, 1, 3, 6, 12, and 16 hours, and 1, 3, 5, 7, and 10 days after the operation.

RESULTS

Insertion of a foreign body into the uterine wall causes destruction of adjacent tissues and extravasation of blood. During the first hours after injury, two morphologically distinguishable zones are formed: a zone of compressed tissue around the wound canal, and an edematous zone which shades gradually into relatively unchanged tissue. This separation into zones remains for 24 hours.

Beginning with the first hour, and sometimes three to six hours after operation, there is a migration, primarily of specialized granulocytes, out of the blood vessels and a movement of these toward the foreign body. After 12-16 hours, macrophages of Maximov's large lymphocyte type are seen, and the number of these increases gradually. Carmine particles introduced with the thread are very quickly phagocytosed by the specialized granulocytes. A small fraction of the dye is found in the macrophages, but on the third to the fifth day some carmine granules are seen in the fibroblasts. The phagocytes with carmine granules in the wall of the uterus are transported in the direction of the broad ligament and are gathered in groups. A similar picture has also been observed by other authors [6]. Henderson [5] has described movement of phagocytes, predominantly macrophages, out of the uterine cavity into the mucosa and into lymphatic formations under the serosa. In some preparations we have been able to see a transfer of individual specialized granulocytes containing carmine, out of the uterine cavity and beneath the epithelial layer.

After 24 hours, a significant fraction of the leukocytes has undergone degenerative changes, and some of the carmine granules are found outside the cells. On the third day after insertion of the foreign body, fibroblastic elements have accumulated around the thread. By the seventh day, giant connective tissue cells are distinctly visible around the fibers of the thread. On the tenth day a significant hypertrophy of all layers of the uterine wall is noted, and a large number of eosinophiles; numerous giant cells, a layer of fibroblasts, and also individual phagocytes have accumulated around the fibers of the inserted thread. Carmine granules are often visible in the giant connective tissue cells.

Analysis of our data showed that in the white rat the rate of phagocytic and regenerative processes in the uterine wall is different at various physiological conditions.

Determination of the phagocytic activity of the specialized granulocytes in the uterine wall during the first

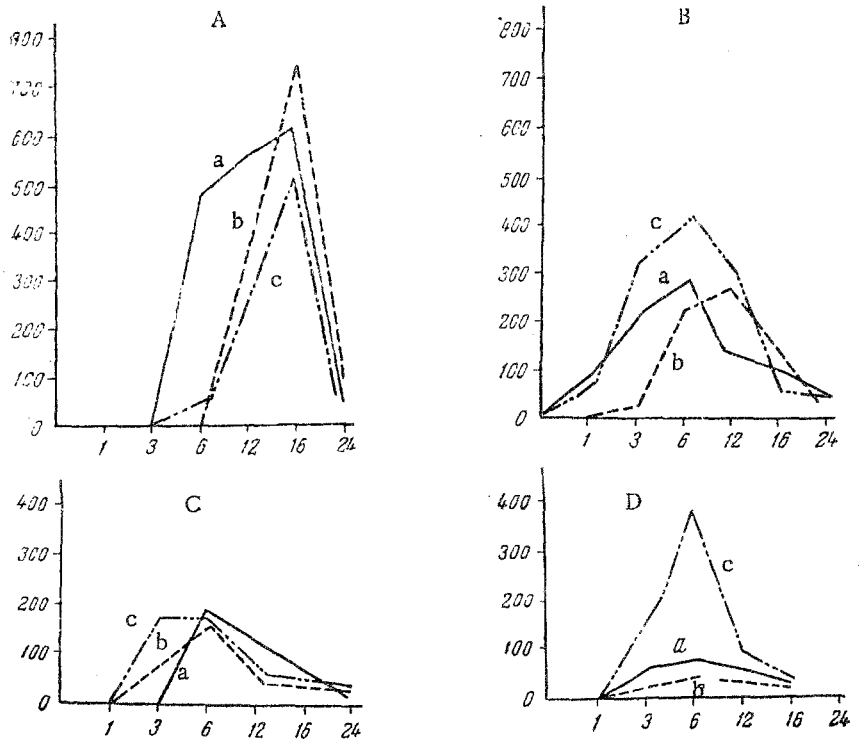

Figure. Changes in the phagocytic activity of specialized granulocytes in tissues of the uterine wall in the white rat. A) 12-day-old rats; B) sexually mature rats (in estrus); C) pregnant rats (on the 7th day); D) immediately post-partum. a – In the uterine cavity; b – in the deep portions of the uterine wall; c – in the uterine serosa. Ordinate) number of phagocytes per 1000 leukocytes; abscissa) hours after operation.

24 hours after insertion of the foreign body resulted in the data shown in the figure.

In the 12-day-old rats (A), the first phagocytes appear three hours after operation. The most intensive phagocytic activity is found after 16 hours. At this time almost all the specialized granulocytes contain carmine granules. After 24 hours many of the specialized granulocytes are dead, and the carmine granules are found outside the cells. It should be noted that in the 12-day-old rats, macrophages showing considerable phagocytic activity accumulate in large numbers around the focus of injury significantly earlier than they do at other ages.

In sexually mature rats (B) during estrus, the transport of specialized granulocytes out of the vessels and the phagocytosis of foreign particles begins earlier than in the 12-day-old rats. Maximum phagocytic activity begins six hours after insertion of the foreign body. Macrophages appear after 24 hours, and in small quantity.

During the period of maximum phagocytic activity, the specialized granulocytes phagocytose only about half of the leukocytes present at the focus of aseptic inflammation.

In mice and rats during estrus, leukocytes in the uterus intensively phagocytose spermatozoa [3]. The introduction of infected sperms into the rabbit uterus during estrus does not cause infection, whereas similar experiments carried out during pseudo-pregnancy do cause infection [4]. The uterus of the cow is resistant to the introduction of a culture of Corynebacterium pyogenes at the time of estrus, but is not resistant when a corpus luteum is present. In this connection it is interesting to compare our data on the phagocytic activity of specialized granulocytes in estrous rats and in pregnant rats. In the figure (C), we find that although in pregnancy the first phagocytes appear, just as in estrus, one to three hours after insertion of the foreign body, and maximum phagocytic activity is observed after six hours, the total number of phagocytes is still very small. Immediately postpartum, phagocytic activity is still further reduced, particularly in the wall of the uterus, although the total number of leukocytes expelled from the blood vessels is extremely large.

The rate of formation of the connective tissue capsule, like the rate of appearance of giant cells, is different in the various stages of ontogenesis. These processes occur very rapidly in 12-day-old rats. In most cases, restoration of a considerable portion of injured tissue has taken place by the third day. Giant cells have appeared around the thread fibers by the fifth day, whereas in sexually mature rats the giant cells are not observed until the seventh to tenth day after operation, and restoration of injured regions and "organization" of the focus of injury occur on the seventh day after the beginning of the experiment. But in analyzing the causes of the more rapid regeneration in 12-day-old rats, we must take into account not only the high phagocytic activity of the specialized granulocytes and macrophages, but also the numerous erythrocytic extravasations that are observed in

the uterine wall when it is injured in various ways, especially in rats of this age. In the vicinity of the extravasated erythrocytes we see lysis of tissue elements, and a considerable disintegration of tissues, which rather quickly is replaced by restoration of the injured areas.

Immediately postpartum, regenerative processes in the uterine wall are somewhat accelerated in comparison with those in nonpregnant animals, but they proceed under such special conditions that it is difficult to analyze them.

It is worth noting that the rates of morphological reactions are different in different parts of the uterine wall, particularly in sexually mature rats.

Specialized granulocytes move quickly out of the vessels of the serosa and the superficial layers of the uterus which line the uterine cavity, and they are actively phagocytic, as is well shown in the figure (B). In the deep layers of the uterine wall, these reactions appear considerably later, although the tissues here are in contact with the foreign body over some distance.

Our data, though preliminary, nevertheless indicate that in the uterine wall of the white rat significant changes in the character of phagocytic reactions are observed with age and with functional states of the sexual apparatus. In studying the roles of individual components of inflammation in form-producing processes in the uterine wall, we must keep in mind the significance not only of leukocytes and macrophages, but also of erythrocytic extravasations and of various complex processes observed in pregnancy and particularly postpartum.

Studies of the reactivity and the possible regenerative reconstruction of uterine wall tissues in the white rate under various physiological conditions provides supplementary material for the analysis of physiological regeneration and of pathological changes of this organ.

SUMMARY

The author studied the course of aseptic inflammation produced by passing a foreign body (sterile cotton thread soaked in carmine) through all the layers of the uterine wall in the white rat.

The phagocytic and inflammatory reactions of the uterine wall showed highly distinctive characteristics in the following groups of rats: 12 days old, $1^1/_2$ months old, sexually mature (in estrus), pregnant (7th-14th day), and immediately postpartum. The rate of formation of the connective tissue capsule was different at various stages of ontogenesis, as was the rate of appearance of giant cells.

Of great importance in the regenerative and inflammatory reactions of uterine wall tissues (especially in 12-day-old rats) are erythrocytic extravasations, which cause temporary tissue disintegration with subsequent rapid regeneration of the injured areas.

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