active hydrolysis of lipid inclusions is observed only in the alveolar macrophages. Mononuclear infiltration of the lungs precedes an increase in the number of alveolar macrophages, which confirms the common source of origin of these cells, which most workers associated with the bone marrow [6-8]. Hydrolysis of the lipids in the interstitial mononuclear cells is at a low level of intensity, which indicates that the cells need to be prepared for this process.

The results of the investigation are evidence of the development of fatty infiltration of the cells. The oil permeates the membranes, penetrates into the cytoplasm and nuclei, and causes injury to them. Destructive changes in the capillaries are the cause of the hemorrhages and microthrombi which, in turn, cause the conditions of function of the cells and tissues to deteriorate sharply and lead to the formation of atelectases together with obstructive lesions of the terminal respiratory passages. The state of the microcirculation plays a leading role also in the development of pneumosclerosis, just as in other lung diseases [1, 4, 5, 10]. An important place in the general combination of factors acting on the inflammatory process evoked in the lungs by a suspension of mineral oil must therefore be ascribed to measures aimed at overcoming the effects of injury to the microcirculation.

LITERATURE CITED

1. Y. D. Batsura, Byull. Éksp. Biol. Med., No. 11, 13 (1970).
2. V. V. Erokhin, "Subcellular morphology of the lungs in experimental tuberculosis," Author's Abstract of Doctoral Dissertation, Moscow (1974).
3. V. V. Erokhin and H. Eckert, Probl. Tuberk., No. 7, 71 (1978).
4. V. V. Serov et al., Arkh. Patol., No. 4, 52 (1972).
5. A. I. Strukov and I. M. Kodolova, Chronic Nonspecific Diseases of the Lungs [in Russian], Moscow (1970).
6. A. Ya. Fridenshtein, Arkh. Anat., No. 4, 3 (1974).
7. D. H. Bowden and I. J. R. Adamson, Am. J. Path., 83, 123 (1976).
8. H. Eckert and S. Jerochin, Z. Erkr. Atm., 150, 34 (1978).
9. R. Furth and J. Thompson, Ann. Inst. Pasteur, 120, 337 (1971).
10. S. F. Ryan, Am. Rev. Resp. Dis., 105, 776 (1972).
11. E. F. Stula and B. K. Kwon, Am. Indust. Hyg. Assoc. J., 39, 393 (1978).
12. I. Weber, Prax. Pneum., 31, 989 (1977).

MORPHOLOGY OF EXPERIMENTAL ACUTE PANCREATITIS DURING TREATMENT WITH 5-FLUOROURACIL

Kh. T. Nishanov and R. I. Kaem

UDC 616.37-002.1-092.9-085.277.3:547.854.4]-091

In experimental pancreatitis induced by a modified method (Arai, 1965) 5-fluorouracil has a marked therapeutic action, preventing the development of necrosis of the acini and suppurative liquefaction of the gland tissue. The authors attribute the therapeutic effect of 5-fluorouracil to its inhibitory action on RNA synthesis and blockade of the liberation of secretion from the exocrine part of the pancreas.

KEY WORDS: acute pancreatitis; 5-fluorouracil.

The treatment of acute pancreatitis still remains a difficult problem in abdominal surgery. The mortality is still extremely high [1, 2]. Several workers [4, 5] have suggested that acute pancreatitis be treated by 5-fluorouracil (5-FU) which, as an inhibitor of RNA synthesis, in the opinion of Martin et al. [6], prevents synthesis in the pancreatic exocrine cells and inhibits secretion of enzymes.

Department of Abdominal Surgery and Department of Surgical Anatomy, A. V. Vishnevskii Institute of Surgery, Academy of Medical Sciences of the USSR, Moscow.

(Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Kraevskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 89, No. 3, pp. 366-368, March, 1980. Original article submitted June 6, 1979.

0007-4888/80/8903-0385$07.50

Fig. 1

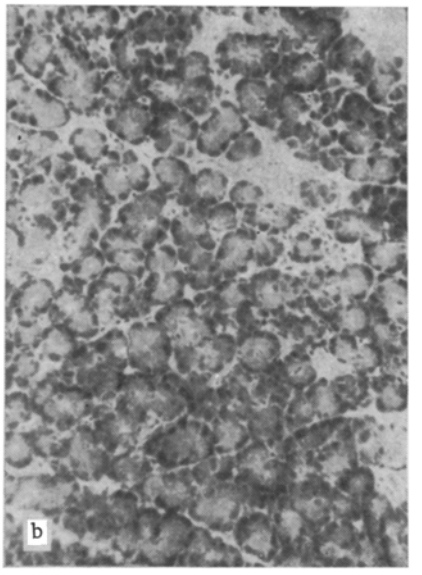

Fig. 2

Fig. 1. Edema and diffuse leukocytic infiltration of interlobular spaces of the pancreas 24 h after beginning of experiment. Hematoxylin-eosin, 80×.

Fig. 2. Preservation of normal architectonics of the pancreas 12 h after beginning of experiment, after injection of 5-FU. Hematoxylin-eosin, 160×.

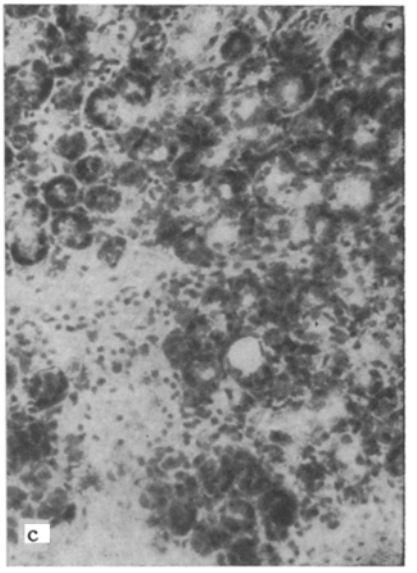

Fig. 3. Decrease in zymogen content in exocrine cells of pancreas. Hematosylin-eosin, 160×.

The object of this investigation was a morphological study of the pancreas in experimental pancreatitis during treatment with 5-FU.

EXPERIMENTAL METHOD

Experiments were carried out on 32 male rats weighing 180-250 g. There were two series of experiments (with 16 rats in each group). Pancreatitis was induced by Arai's method [3] by ligation of the common bile duct at the point where it empties into the duodenum, with

simultaneous stimulation of secretory function of the gland by injection of 0.7% pilocarpine solution in a dose of 0.01 g/kg body weight. The animals of series II were given an intraperitoneal injection of 5-FU in a dose of 4.5 mg/100 g body weight at the end of the operation. The rats were killed 6, 12, 24, and 96 h later. The pancreas was fixed in 10% neutral formalin and embedded in celloidin. Sections were stained with hematoxylin and eosin.

EXPERIMENTAL RESULTS

In the experiments of series I (control) congestion of the vessels and capillaries, edema of the interlobular and interacinar spaces, with migration of a few polymorphs into the edema fluid, were observed in the animals after 6 h. The lumen of the glandular tubules and efferent ducts were dilated and filled with eosinophilic secretion. Foci of necrosis of gland tissue were detected in individual lobules. Edema of the gland tissue intensified after 12 h. The number of foci of necrosis of the acinar tissue increased. Accumulation of polymorphs was observed in the interlobular spaces. The number of zymogen granules in the gland cells remained high. Foci of necrosis and suppuration were found in the surrounding adipose tissue. The number of necrotic and degeneratively changed acini rose sharply after 24 h and large foci of necrosis were seen. Interstitial edema was observed, with abundant diffuse leukocytic infiltration of the interlobular and interacinar septa (with signs of bacterial invasion). The efferent ducts were dilated and filled with secretion, their walls were infiltrated with polymorphs, and pyophlebitis, foci of necrosis, and abscess formation in the surrounding adipose tissue were observed (Fig. 1). Diffuse-focal necrosis of the tissue of the pancreas with a few preserved acini was observed after 96 h. The interlobular and intracinar spaces were widened and filled with exudate contaminated with a few neutrophils, monocytes, and eosinophils.

In the experiments of series II (experimental series) 6 h after the operation moderate edema of the interlobular spaces of the gland was found. The zymogen content in the gland cells was within normal limits, but a little reduced in places. The efferent ducts contained little or no secretion. Exudate filling the interlobular spaces contained numerous cells: polymorphs, macrophages, and monocytes. Moderate congestion of the vessels and capillaries was observed in the adipose tissue surrounding the gland (Fig. 2). Signs of moderate congestion of the vessels and capillaries were still present in the gland after 24 h. The intensity of the edema of the interlobular spaces was reduced. The architectonic structure of the acini was normal. The cytoplasm of the exocrine cells was stained pale pink, indicating some decrease in the zymogen content of the cells. Foci of destruction in the gland tissue were not present. The interlobular spaces contained many round cells and a few polymorphs. After 96 h the zymogen content in the cells of the pancreatic acini was reduced a little. The architectonics of the gland was completely preserved. Only moderate congestion of the vessels of the gland and of the surrounding adipose tissue could be seen. Single round cells were detected in the interlobular spaces. The efferent ducts and lumen of the glandular tubules contained no secretion (Fig. 3).

The results of the present investigation indicate that administration of 5-FU prevents the development of suppurative necrotic pancreatitis. After treatment with 5-FU foci of necrosis and suppurative infiltration are not found in the gland tissue and the quantity of secretion in the gland cells is appreciably reduced. Comparison with data in the literature [5] shows that 5-FU is a powerful inhibitor of RNA and DNA synthesis, and since it also blocks the outpouring of secretion it is a highly effective therapeutic substance.

LITERATURE CITED

1. G. N. Akzhigitov, Acute Pancreatitis [in Russian], Moscow (1974).
2. V. S. Savel'ev et al., Textbook of Emergency Abdominal Surgery [in Russian], Moscow (1975).
3. T. Arai, Proc. Soc. Exp. Biol. (New York), 119, 4 (1965).
4. R. M. Johnson et al., Am. J. Surg., 125, 211 (1973).
5. V. Kinami et al., World J. Surg., 2, 881 (1978).
6. B. F. Martin et al., J. Anat. (London), 104, 93 (1969).