The histological studies confirmed changes in structure of the megaureteric wall: various degrees of myofibrosis, perimuscular sclerosis, sclerosis of the laminar propria of the urothelium, were found in the region of "devitalization"; single smooth-muscle cells or groups of them were in a state either of atrophy or of hypertrophy to a varied degree. Signs of perimuscular sclerosis were seen in segments of the ureters above the devitalization. Evidence of hydronephrosis and nephrosclerosis, culminating in secondary contracted kidney, were observed.

Thus the study demonstrated the possibility of creating a model of megaureter in dogs by injuring a segment of the ureter. The formation of nonobstructive megaureter in 41% of experiments with devitaliation of a segment of the upper third of the ureter demonstrates the important role of a functional stricture — without anatomical narrowing — in the pathogenesis of this threatening syndrome. Formation of obstructive megaureter in 100% of cases in experiments with devitalization of the ureterocystostomy can probably be explained by the anatomic and functional characteristics of this part of the urinary tract, and it is in agreement with the fact that strictures are observed more frequently in the lower part in patients with megaureter.

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CHANGES IN THE PERITONEUM OF THE SMALL INTESTINE AND DIAPHRAGM IN EXPERIMENIAL PORTAL HYPERTENSION

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Normally balanced secretion and absorption of fluid takes place constantly in the peritoneal cavity, so that the quantity of fluid remains stable [2, 4]. The intensity and direction of circulation of fluid are maintained by the activity of the different parts of the peritoneum, whose structural organization has been adequately studied [1, 3, 6-8]. Portal hypertension (PH), a complication of several diseases of the digestive and cardiovascular systems, is accompanied as a rule by an increase in the quantity of free fluid in the peritoneal cavity, or ascites [5], which develops as a result of predominance of transudation over resorption. Our knowledge of the pathogenesis of ascites at the present time does not give a clear idea of the role of changes in the regions of the peritoneum responsible for transudation and resorption, or of its formation.

The aim of this investigation was to study morphological changes in various parts of the peritoneum and, in particular, that covering the small intestine, through which transudation takes place, and the diaphragmatic peritoneum, responsible for resorption of fluid from the peritoneal cavity.

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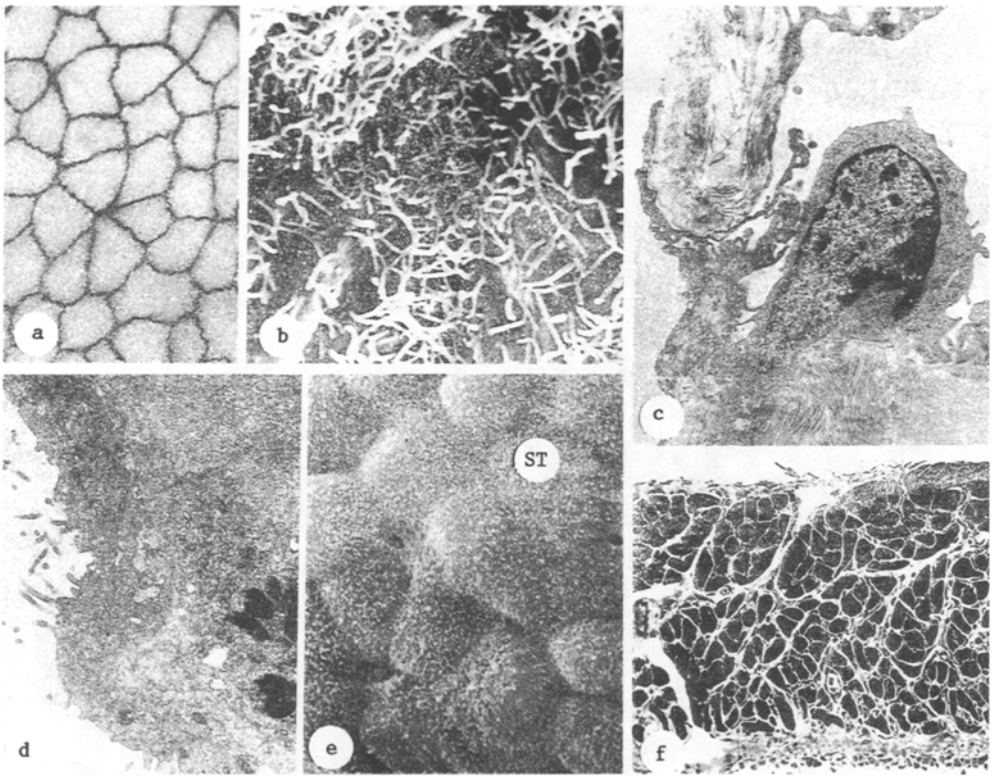

Fig. 1. Structure of peritoneum covering small intestine and diaphragm under normal conditions: a) boundaries between mesotheliocytes; b) surface microrelief of mesotheliocytes; c) tight junctions between mesotheliocytes (J); d) microrelief of resorbing part of peritoneum (diaphragmatic), orifices of stomata (ST); e) zone of junction of endotheliocytes of lymphatic lacuna (E) with mesotheliocytes (MC); f) subpleural lymphatic collector (arrow). a) Impregnation of cell boundaries, 400×; b and d) SEM, magnification 5000 and 700; c and e) TEM, magnification 10,000 and 6000.

EXPERIMENTAL METHOD

Supradiaphragmatic stenosis of the inferior vena cava by 50% was carried out on 24 male Wistar rats weighing 150-175 g, under ether anesthesia. The animals were killed by instant decapitation 3, 7, 14, and 30 days later. Areas of the diaphragm and small intestine, after appropriate treatment, were examined in scanning (SEM) and transmission (TEM) electron microscopes. Semithin sections were stained with a mixture of 1% solution of methylene blue and fuchsine. The boundaries between the mesothelial cells were impregnated with a 0.25% solution of silver nitrate and then fixed in a 4% solution of formaldehyde in order to obtain two-dimensional preparations. Areas of peritoneum taken from six intact animals served as the control.

EXPERIMENTAL RESULTS

In intact animals the peritoneum of the small intestine is lined with a continuous layer of mesothelial cells with smooth and clear intercellular boundaries (Fig. 1a). Numerous long, branched microvilli are located on their apical surface (Fig. 1b). The mesotheliocytes are flat in shape and located on a continuous basal membrane, and their cytoplasm contains pinocytotic vesicles. Both tight and gap intercellular junctions are present (Fig. 1c). Microvessels (capillaries and postcapillary venules) are present in the connective-tissue base in the immediate vicinity of the basal membrane.

The mesotheliocytes of the resorbing ports of the diaphragmatic peritoneum are much smaller and the boundaries between them thicker. Openings (stomata), from 1 to 4 μ in diameter, lie between groups of cells. The apical surface of these mesotheliocytes contains occasional short microvilli (Fig. 1d).

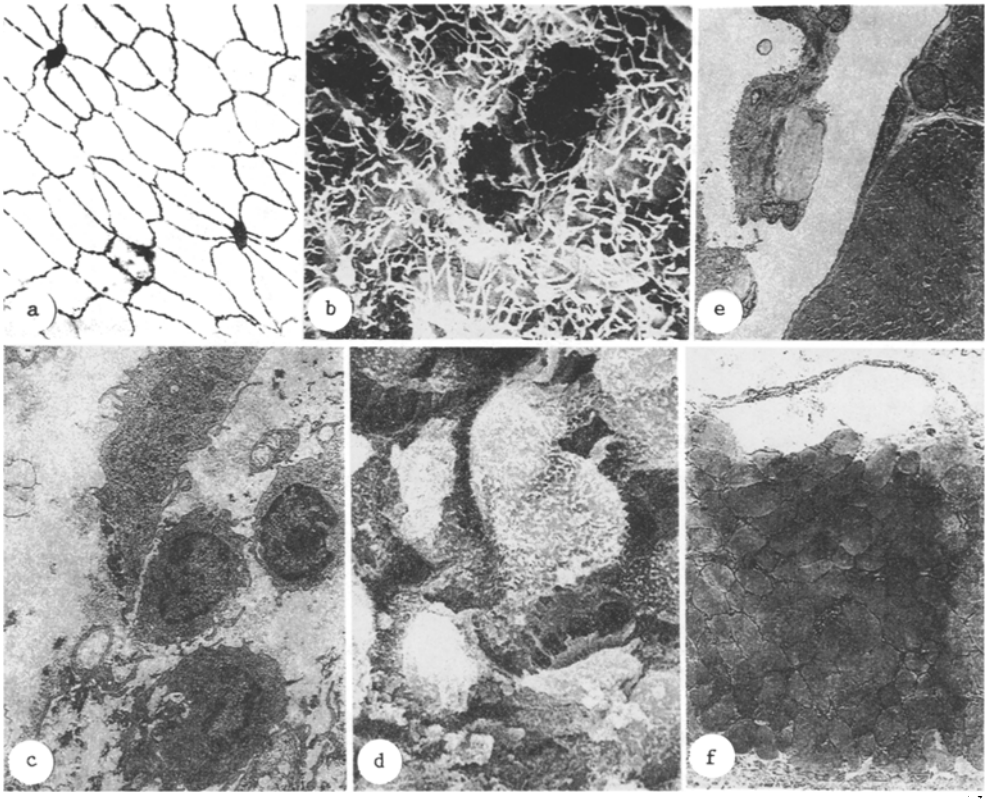

Fig. 2. Morphology of small intestinal and diaphragmatic peritoneum in portal hypertension with ascites: a and b) appearance of stomata between mesotheliocytes (arrow); b) separation of mesotheliocytes with widening of intercellular spaces. Peritoneal edema; d) increase in diameter and number of stomata in diaphragmatic peritoneum; e) direct communication between lumen of lymphatic lacuna and peritoneal cavity. a) Impregnation of cell boundaries, 400×; b and d) SEM, magnification 3000 and 1000; c and e) TEM, magnification 4000 and 1500; f) semithin section stained with methylene blue and fuchsine, 100×.

Directly beneath the mesothelium lie lymphatic lacunae, whose endotheliocytes are in contact with the lateral surfaces of the mesotheliocytes in the region of the stomata, forming distinctive cellular valves (Fig. 1e). In these areas fluid is resorbed into the lymphatic system. The fluid thereafter enters a network of lymphatic vessels located beneath the diaphragmatic pleura (Fig. 1f). Under normal conditions the diameter of the lymphatic lacunae is 48 ± 8.6 μ and that of the lymphatic collectors 270 ± 18 μ.

In the early stages of PH (3-7 days) the peritoneal cavity of the animals contained from 0.5 to 1.0 ml of fluid. Impregnation of the intercellular boundaries of the small intestinal mesotheliocytes revealed very slight widening. The apical surface of the cells became convex in shape, the number of microvilli was the same as before, but the degree of pinocytosis was increased Marked edema developed in the submesothelial space, The lumen of the peritoneal microvessels was widened.

The characteristic shape of the mesotheliocytes of the diaphragmatic peritoneum was close to cubical, the intercellular boundaries were correspondingly widened, and the number and diameter of the stomata increased (4.4 ± 0.18 μ). The lumen of the lymphatic lacunae and lymphatic collectors also was widened (71 ± 11.2 and 350 ± 24 μ).

Later (14-30 days) the volume of ascites fluid was 3-5 ml. The mesotheliocytes were cubical in shape and the intercellular boundaries greatly widened. Circular holes resembling stomata, from 4 to 18 μ in diameter, appeared between groups of cells (Fig. 2a, b). The number of microvilli was reduced and floccules of fibrin and erythrocytes could be seen on the surface of the mesotheliocytes (Fig. 2b). The ultrastructural changes were characterized by high pinocytosis and intracellular edema. Intercellular junctions did not contain junction complexes, and the cell edges lay a considerable distance apart. The basal membrane also lost its continuity (Fig. 2c). Marked edema was present in the connective-tissue base of the peritoneum, and deposits of fibrin and free erythrocytes were observed. The lumen of the capillaries and postcapillary venules was greatly dilated and their endothelium fenestrated. The number of microvessels increased and they were arranged directly under the mesothelial layer.

An increase in the number and diameter of the stomata (up to 12 μ) of the resorbing ports also was found in the diaphragmatic peritoneum. The mesotheliocytes contained fewer microvilli and the intercellular boundaries were greatly widened. Most lymphatic lacunae were in direct communication through the dilated openings of the stomata with the lumen of the peritoneal cavity (Fig. 2e). The structure of the valvular formations described above was disturbed. The diameter of the lymphatic lacunae and of the lumen of the lymphatic collectors was sharply increased compared with the earlier period, to 120 ± 11 and 1200 ± 138 μ respectively (Fig. 2f). In some cases the lumen of the lymphatic lacunae and collectors was obliterated with erythrocytes and fibrin.

Thus in the early stages of PH morphological changes indicating intensification of transudation of fluid into the peritoneal cavity are found in the small intestinal peritoneum: dilatation and congestion of the exchange microvessels of the peritoneum, edema of the interstitial tissues, widening of the intercellular spaces, and intensification of pinocytosis. In the resorbing parts of the peritoneum, signs of intensive entry of fluid into vessels of the lymphatic system are an increase in the diameter and number of the stomata of the resorbing ports of the diaphragm and a considerable degree of widening of the lumen of the lymphatic lacunae and collectors. As PH progresses, openings appear between the mesotheliocytes, with fenestration of the basal membrane. This severe disturbance of the barrier properties of the periteneum leads to the outflow of fluid into the peritoneal cavity, accompanied by fibrin and erythrocytes. Compensatory changes in the resorbing areas consist of marked dilatation and an increase in number of the stomata, and direct communication between the lumen of the lymphatic lacunae and the peritoneal cavity.

Under these conditions decompensation of the function of the resorbing areas very quickly develops, and is based on factors such as the increased inflow of fluid, disturbance of function of the cellular valves due to the marked dilatation of the stomata, and also obliteration of the lumen of the lymphatic lacunae and collectors by erythrocytes and fibrin.

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