

of the epitheliocytes were moderately widened. Capillary endotheliocytes in the zone of contact with the epitheliocytes formed multiple fenestrations over a large area (Fig. 1d, e). Structural changes discovered in the epitheliocytes and the capillary network indicates an enhanced absorptive function.

The results are thus evidence that, if nutrient mixtures of equal and high calorific value, providing 1 kcal/ml of solution, are given optimal conditions, maintaining "coordination" between absorption of all nutrients are created if the calorific value is increased, as a result of an increase in the content of the basic nutrients so that they correspond to their proportions in the chyme, and a constant ratio is maintained between poly-, oligo-, and monomers. Preference must be awarded to mixtures of such a composition when total enteral feeding of surgical patients is indicated.

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#### INVESTIGATION OF EXPERIMENTAL STAPHYLOCOCCAL SEPSIS

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KEY WORDS: sepsis; experimental model.

Despite active research into the problem of sepsis, conflicting opinions are still held on aspects of its pathogenesis, there is no generally accepted terminology and classification, and should the disease arise its mortality remains high. Prospects for the solution of this problem rest on expansion of fundamental theoretical ideas of the nature of this disease and, in particular, the study of microorganism-host interrelationships, which will enable up to date clinical-bacteriologic and morphologic criteria of the development of this infectious process to be established [4].

A detailed study of the mechanism of these interrelationships is possible only experimentally. However, it has not yet proved possible to induce sepsis in animals by introducing bacteria isolated from man. Existing methods reproduce either bacteriemic shock [3] or local suppurative infection with periodic bacteriemia [5]. The main shortcoming of all known methods is the absence of a set of criteria whereby sepsis can be characterized as an independent disease.

In the investigation described below the development of the principal features of sepsis was studied using rats as the model.

#### EXPERIMENTAL METHOD

Experiments were carried out on 230 mature noninbred male albino rats. The infectious process was induced by a single intramuscular injection of various doses of a culture of

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TABLE 1. Mortality among Animals (in %) Depending on Their Weight after Intramuscular Injection of a Suspension of Staphylococci in CaCl<sub>2</sub> Solution

Group of animals	Time of experiment, days					Total
	1	1-3	4-7	8-20	21-45	
Rats weighing 120-140 g (n=100)	2	3	11	4	8	28
Rats weighing 300-350 g (n=100)	1	2	2	3	1	9

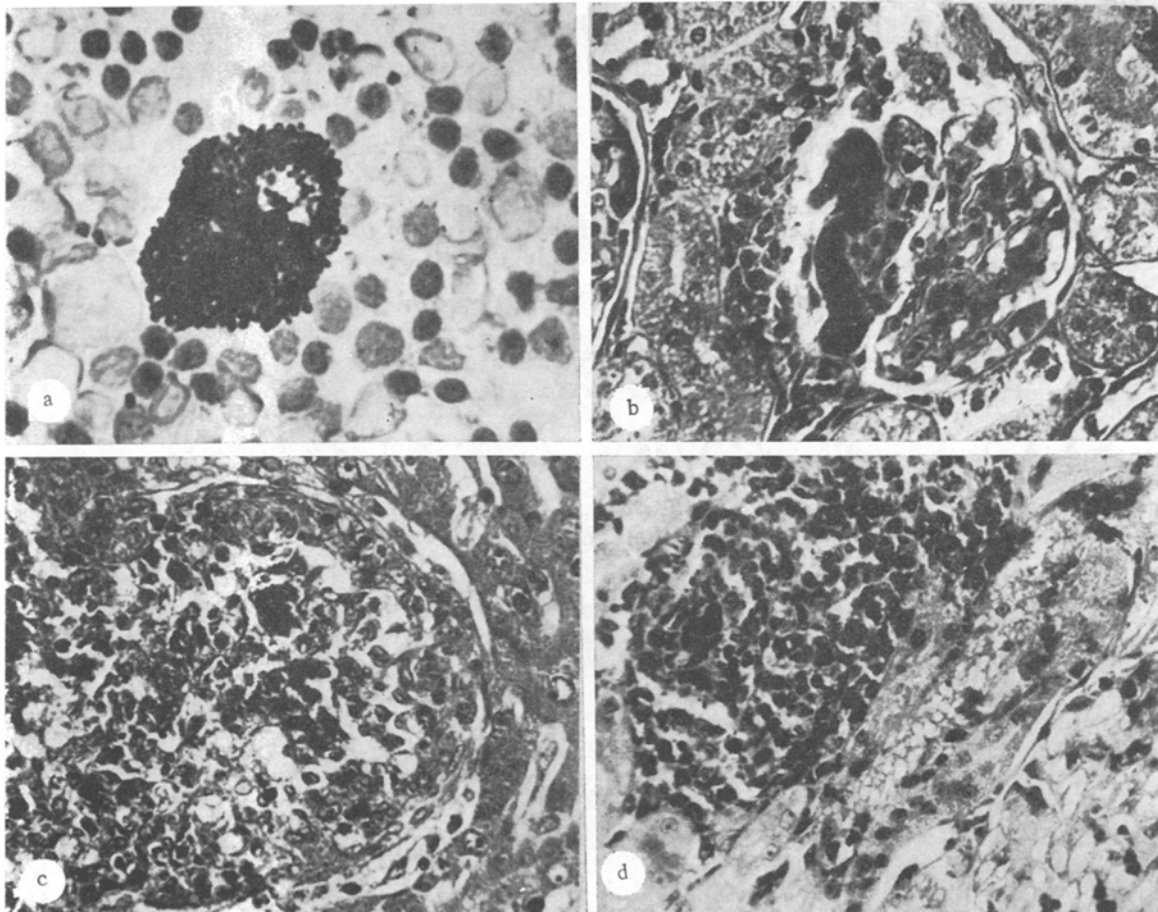


Fig. 1. Morphologic manifestations of experimental staphylococcal sepsis in rats: a) colony of staphylococci in squash preparation of spleen. Remonovsky-Giemsa stain. 600 ×; b) septic embolus in capillary of renal glomerulus. Loeffler's blue and eosin. 252 ×; c) metastatic focus in liver. Loeffler's blue and eosin. 120 ×; d) metastatic focus in kidney. Loeffler's blue and eosin. 400 ×.

*Staphylococcus aureus* isolated from patients with sepsis, in 10% CaCl<sub>2</sub> solution: young animals weighing 120-140 g received 0.15 ml, rats weighing 300-350 g received 0.3 ml, of a suspension containing 10<sup>15</sup> bacterial cells in 1 ml. Control animals received the corresponding dose of bacteria in physiological saline.

The internal organs of animals which died or were killed in the agonal state between the 1st and 45th days after injection were fixed in Carnoy's fluid: Tissue was embedded in paraffin wax and sections stained with hematoxylin and eosin and with Loeffler's blue and eosin. Squash preparations of the liver, kidneys, spleen, and serous surface of the peri-

toneum, and blood films were stained by the Romanovsky-Giemsa method. Blood and squash preparations of the parenchymatous organs were seeded and a total blood count done.

#### EXPERIMENTAL RESULTS

Injection of a suspension of microorganisms in physiological saline into the hind limb muscle caused a local infectious process to develop in the control rats, accompanied by bacteriemia, manifested as positive results of seeding the internal organs. However, the process subsided in the course of 3 or 4 days and all the animals recovered.

Injection of the suspension of microorganisms in  $\text{CaCl}_2$  solution was accompanied by local tissue necrosis, inhibition of the reparative reaction, and simultaneous infection. As a result, unlike in the control, the local suppurative inflammatory process continued to develop, and after 4-5 days a superficial ulcer was formed, the exudate from which contained leukocytes and staphylococci.

Some of the affected animals died (Table 1). The mortality in the group of young rats weighing 120-140 g was almost three times higher than in the group of older animals. The local infectious focus disappeared in the remaining rats and after 2-2.5 months the ulcers became cicatrized.

Bacteriemia developed in all the infected rats during the 1st-3rd days of the disease, and was shown by the appearance of positive blood cultures and dissemination of infection among the internal organs. Colonies of staphylococci were found mainly in squash preparations of the spleen (Fig. 1a), to a lesser degree in similar preparations from the liver and kidneys, and also the serous surface of the peritoneum.

Subsequent development of the infectious process led to the appearance of qualitatively new features of the disease. Blood taken from animals in an agonal state did not clot for a long time. Its analysis revealed marked normochromic anemia, manifested as a fall in the hemoglobin concentration from  $107 \pm 2.6$  g/liter in the control to  $60.7 \pm 2.3$  g/liter in the experiment ( $P < 0.01$ ), and a fall in the erythrocyte count from  $(2.19 \pm 0.012) \cdot 10^{12}$ /liter in the control to  $(1.03 \pm 0.016) \cdot 10^{12}$ /liter in the experiment ( $P < 0.001$ ). Slight leukopenia [ $(10.9 \pm 0.51) \cdot 10^9$ /liter in the control,  $(9.3 \pm 0.62) \cdot 10^9$ /liter in the experiment ( $P > 0.01$ )], neutrophilia (3 times higher than in the control), a marked shift toward stab cells and juvenile forms of neutrophils, and the virtually total absence of eosinophils were observed.

At autopsy hyperplasia of the spleen, multiple foci of necrosis, and dystrophic changes in the parenchyma of the liver and kidneys, pneumonic foci, in some places hemorrhagic in character, in the lungs, and foci of subepicardian hemorrhages and signs of myocardial dystrophy were found.

If the disease followed a more severe course suppurative foci were found in the subcutaneous connective tissue, and miliary abscesses were present on the surface of the internal organs and peritoneum. Histological investigation revealed septic emboli in the lumen of the small vessels and metastatic suppurative foci in the parenchyma of the liver and kidneys, and also in the myocardium (Fig. 1, b-d).

Sepsis in man is associated with the appearance of a combination of the following criteria: the presence of a local infectious focus and of bacteriemia, the formation of foci of necrosis and dystrophic changes in the internal organs, and the appearance of secondary pyemic foci in them. Finally, at present the disease is associated with definite mortality [1, 2]. The combination of similar features observed in rats after receiving an injection of a suspension of bacteria in  $\text{CaCl}_2$  solution indicates that this model provides the closest possible approach to criteria of sepsis as manifested in man.

It can be postulated on the basis of this investigation that just as in man [4], the course of sepsis in rats goes through successive phases of development from the formation of a local suppurative focus and of bacteriemia in the initial stages to septicemia, with evidence of bacteriemia, destructive and dystrophic changes in the organs, and septicopyemia, combining the features of septicemia with metastatic suppurative foci in the organs in the final stages of the infectious process.

The animals die in different stages of development of sepsis, and mortality is higher among young than among more adult rats; this is evidently attributable to differences in the immune status of the organism.

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