marked hyperplasia and hypertrophy of the mitochondria are evidence of an increase in their energy-producing ability [4]. Hepatocytes of the second type appeared less electron-dense because they contained structureless zones, as well as swollen mitochondria with translucent matrix and disoriented cristae. The cytoplasm also contained mitochondria with a denser matrix and with regularly oriented cristae. The most characteristic feature of these cells was the development of elements of the RER and SER. In some places transition of the RER into the SER was observed, accompanied by removal of ribosomes from the membranes (Fig. 3). Considering that the function of SER is to take part in metabolism of foreign chemical substances [5], we consider that the most important role of these cells is to weaken the action of toxic metabolites on the affected liver.

The results of these investigations thus show that repair processes in chronic hepatitis cannot compensate for the death of large areas of the parenchyma. Administration of benzonal promotes the reversibility of the process due to the considerable activation of cellular and, in particular, of intracellular processes, as is confirmed by the presence of cells of two types: cells with enhanced energy potential, and cells eliminating toxic metabolites more quickly.

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EXPERIMENTAL CANDIDIASIS OF THE ORAL MUCOSA DURING INHIBITION OF LEUKOPOIESIS

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KEY WORDS: candidiasis; leukopoiesis; necrosis

The number of patients with visceral forms of candidiasis has risen steadily in recent years, probably due both to the widespread use of modern therapeutic substances and to the prevalence of severe underlying diseases on the basis of which this mycotic condition frequently develops [3-5, 7]. The tissue response to introduction of conditionally pathogenic fungi of the *Candida* genus has a wide spectrum of morphological manifestations [4-7], and the predominance of an acellular inflammatory reaction in a certain category of patients is probably linked with the corresponding immune status. Acellular or inert inflammation is characterized by the absence of typical inflammatory cells within the pathological focus. An important component of this type of reaction may be necrosis [6]. However, the morphology and morphogenesis of this variant of inflammation have not been adequately studied.

In the investigation described below, on an experimental model of candidiasis of the oral mucosa accompanying administration of the antibiotic tetracycline and the cytostatic vinblastine sulfate, the character of development of the acellular inflammatory reaction was studied at the tissue and ultrastructural levels.

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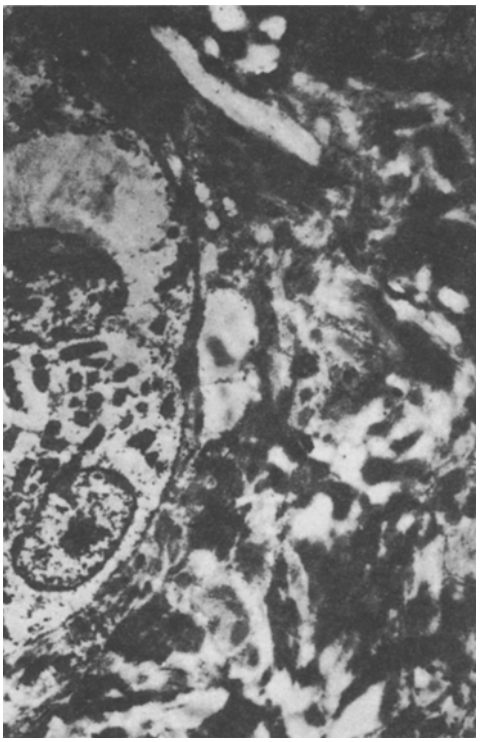

Fig. 1. Lamina propria of oral mucosa on 15th day of experiment. Edema, fibrinoid necrosis. 6000×.

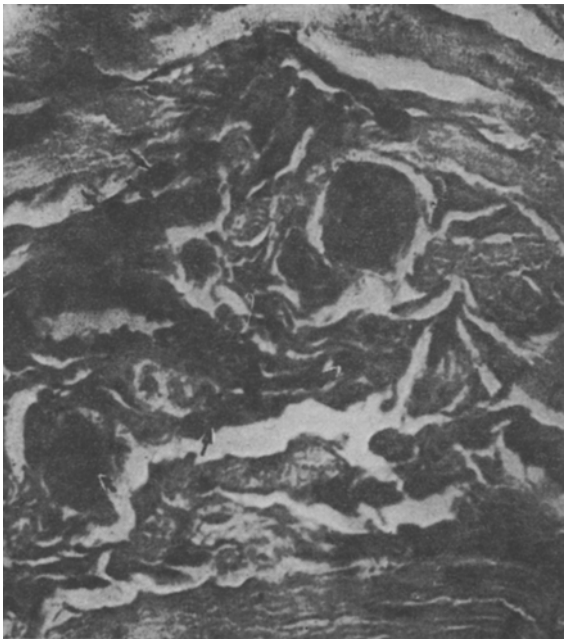

Fig. 2. Muscular layer of tongue on 17th day of experiment: blastopores of yeast-like fungi of the genus *Candida* (arrows). Gram–Weigert stain. 200×.

EXPERIMENTAL METHOD

Experiments were carried out on two groups of male albino rats weighing 110-120 g (25 experimental and 15 control animals). For 2 weeks the rats of both groups were given intramuscular injections of tetracycline hydrochloride (total dose for the course 0.56 g), and rats of the experimental group also received vinblastine sulfate (total dose for the course 0.0222 mg). The drugs were discontinued on the 14th day of the experiment and a suspension of the

Fig. 3. Perivascular edema, 17th day of experiment: fibrin threads (F) outside a congested vessel. Gram–Weigert. 400×.

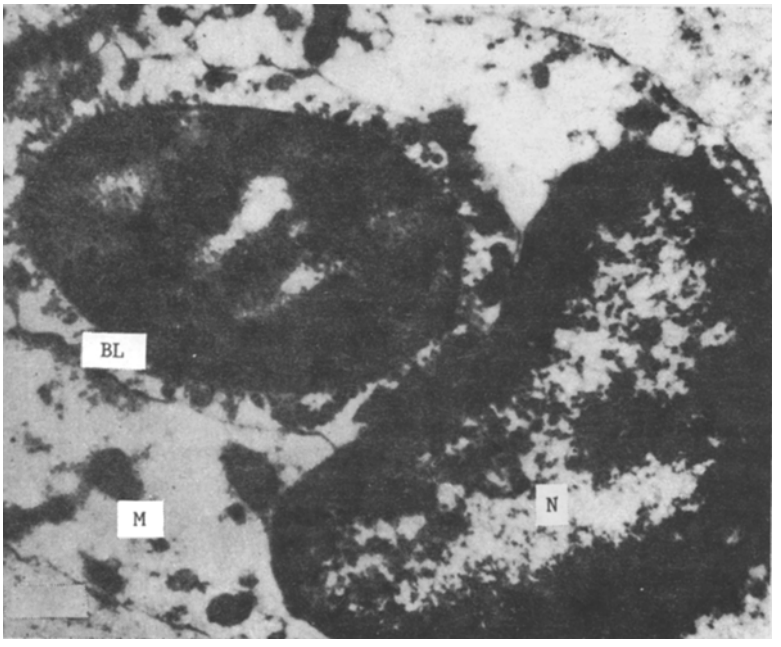

Fig. 4. Phagocytosis of fungal cell. 20th day of experiment. Blastospore (BL) in contact with nucleus (N) of macrophage (M). 10,000×.

fungus *C. albicans* (10^6 cells/ml according to an optical standard of turbidity, made up after counting in a Goryaev's chamber), was added to the diet. The results of infection with the fungus were assessed on the 14th, 15th, 17th, 20th, and 24th days of the experiment by mycologic, histologic, and electron-microscopic methods (five animals at each time from the experimental and three from the control groups). The dorsal part of the tongue was studied [8]. Material from this region was seeded on Sabouraud's agar, and pieces of tissue for histologic study were fixed in a 10% solution of neutral formalin, and for electron microscopy in a 4%

solution of glutaraldehyde with the addition of dimethyl sulfoxide [1]. The sections were stained with hematoxylin and eosin, and for determination of the fungal flora by the Gram–Weigert method.

EXPERIMENTAL RESULTS

No morphological changes could be found in the mucosa and underlying tissues at any time of the investigation in animals of the control group. Mycologic investigation of this same material, cultured from the superficial layer of the epithelium, was positive at all times, and this was interpreted as a carrier state of candidiasis.

A carrier state for the fungus was detected in animals of the experimental group as early as 5 h after the beginning of feeding with *C. albicans* (the 14th day of the experiment), and later the mold invaded the underlying tissues of the tongue, with the development of an inflammatory process.

On the 15th day of the experiment the inflammatory reaction was alterative in character. Degenerative and necrotic changes not only were observed in the surface epithelium and the underlying connective tissue, but they also spread to individual muscle cells of the tongue. Histologic investigation revealed colonization of the surface of the epithelium by *C. albicans* within the stratum corneum, with large numbers of budding blastospores and the formation of single growth tubes of pseudomycelium, and inflammatory hyperemia of the vessels of the lamina propria of the lingual mucosa. At the ultrastructural level, areas of fibrinoic necrosis were seen in the latter structure, in the form of disorganization of collagen fibers and deposition of fibrin (Fig. 1), whereas in the muscular layer of the tongue there were destructive-necrobiotic changes in the form of swelling and homogenization of the mitochondria with fragmentation and destruction of their cristae. Disturbance of the typical ultrastructure was seen in individual muscle bundles: absence of dark bands (Z disks), which normally connect the myofibrils with the cytoplasmic membrane (sarcolemma).

On the 17th day of the experiment and the 4th day of administration of *C. albicans* with the food, retroculture in animals of the experimental group was positive and gave continuous growth of the pathogen. Morphologically, the fungus was observed to be invading the muscular layer of the tongue through the porous basement membrane of the epithelium (Fig. 2). Degenerative and exudative changes predominated: serous edema, deposition of fibrin (Fig. 3), in the absence of the traditional diapedesis of polymorphonuclear leukocytes into the pathological focus, probably due to the suppressive effect of the cytostatic on leukopoesis.

On the 20th day of the experiment completion of phagocytosis of the fungal cells by macrophages was associated with repair processes in the tissues of the tongue. Seedings from the deep layers of the tongue in animals of the experimental group were positive, but the number of colonies did not exceed 15 on average in each tube. Histologic investigation revealed reparative regeneration in the form of an increase in the number of mitoses in the epithelial cells and hypertrophy of the muscle cells on account of hyperplasia of intracellular structures. Single blastopores of *C. albicans* were found in the neighborhood of small foci or infiltrating cells, consisting mainly of histiocytes and macrophages. At the ultrastructural level some macrophages contained fungal cells (Fig. 4) or their fragments in their cytoplasm.

On the 24th day of the experiment and the 11th day after the beginning of feeding with *C. albicans*, fungal structures were no longer detected in the lingual tissues, and the animals made a complete recovery.

The acute inflammatory reaction to infection with the fungus *C. albicans* thus has regular patterns and phases of development. However, it is distinguished by predominance of a degenerative–exudative component, in the form of tissue necrosis, serous edema, deposition of a fibrin network, and absence of diapedesis of leukocytes into the pathological focus. The development of this kind of inflammatory reaction to invasion by fungi in patients with leukopenia was also observed by Ayers et al. [6]. The acellular character of the inflammation evidently prevented the spread of blastospores in the pathological foci into pseudomycelial structures [4] in our own experiments.

Inhibition of leukopoiesis by the cytostatic evidently led to the acquisition of lysosomes, characteristic of polymorphs, by the monocytic macrophages. The heterolysosomal nature of the phagocytes during a predominantly necrotic reaction in the tissue has been suggested by Pigarevskii and Tolybekov [2]. The particular feature of macrophages in degenerative and necrotic tissue reactions, observed by these authors, probably determined the phasic

character of the inflammatory process in the present investigation, with transition from the exudative-necrotic stage into the proliferative stage. In the present experiments, it was evidently this functional integrity of the monocytic macrophages which determined the completed character of phagocytosis and the favorable outcome of the inflammatory process.

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LIMITS OF ULTRASTRUCTURAL HOMEOSTASIS IN SKELETAL MUSCLES UNDER NORMAL CONDITIONS AND DURING MUSCULAR ACTIVITY

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KEY WORDS: homeostasis; skeletal muscles; regeneration

Modern views on the structural basis of homeostasis have been developed by Academician of the Academy of Medical Sciences of the USSR, D. S. Sarkisov [4, 5]. The principles of the supply of materials required for function, which he has argued, stipulate precisely that a change in function of any organ within normal limits is determined by variation of the number of its working structural units. A rapid increase in functional load is possible due to an increase in mass of the working organs or systems of organs [12]. This process, the material basis of adaptation, takes place through hyperplasia of its components [7]. The increase in their number, moreover, may take place at both cellular and intracellular levels [6]. Three forms of adaptive increase in the number of structural components of intensively working organs are distinguished: the first is based on new cell formation, the second on a roughly equal increase in numbers both of cells and of intracellular components, and the third on intracellular regeneration alone [5].

Considering the traditional views on hypertrophy of skeletal muscles during intensive physical exertion (PE) the following question naturally arises: on account of an increase in number of what structure does the mass of the working muscle increase? Accordingly, the aim of this investigation was to determine the limits of fluctuations in the number of dominant ultrastructures of skeletal muscles under normal conditions and during intensive PE.

EXPERIMENTAL METHOD

Experiments were carried out on 162 male albino rats aged 1, 3, and 12 months. PE, in the form of running on a treadmill, took place for 20, 40, 60, and 90 days at a speed of 45 m/min. Rats of the same age, kept under animal house conditions, served as the control. After decapitation, pieces of the pectoralis major (PM) and latissimus dorsi (LD) muscles were excised. Material was prefixed in 4% glutaraldehyde solution, postfixed in 1% OsO_4 solution, and embedded in a mixture of Epon and Araldite. The sections were stained with uranyl acetate

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