# Asymmetry During Regeneration of Microvessels in Rabbit Ear

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General principle of development, the left-to-right gradient of maturation, is valid for the regeneration of microvessels in rabbit ear. This manifests itself in a more rapid regeneration of microvessels of the left ear. The right ear is characterized by excessive regeneration which then decreases to the normal. Dalargin has different effects on microvessels in different ears: in the left ear the peptide inhibits revascularization, while in the right ear it accelerates the process of revascularization.

**Key Words**: *microvessels; morphometry; regeneration; dalargin; asymmetry*

Studies devoted to the tissue regeneration or formation during ontogeny usually ignore the peculiarities of these processes in paired organs. The only exception is the brain (due to marked functional differences between symmetrical regions). Therefore, brain studies have established the general principle of the development: left-to-right gradient of maturation, which reflects a more rapid maturation of the left side and an earlier specialization of the left hemisphere [1,2,7].

The aim of the present study was to verify this principle for maturation of newly formed microvessels in paired organs, specifically, for regenerating vessels of the rabbit ear perichondrium.

## MATERIALS AND METHODS

Regeneration of microcirculatory bed (MCB) was monitored after implantation of transparent chambers into rabbit ears. The rabbit ear chamber technique is now a routine method for study of microvessels; it was previously applied by us with some modifications [6]. Group I consisted of 6 rabbits weighing 2.5±0.1 kg. Twelve chambers were implanted with 6 fixed observation areas in each. The implantation was performed under Nembutal anesthesia (40 mg/kg, rectally). Light microscopy (×50) was performed without anesthesia. Microvessels were examined on days 21, 23, 25, 28, 30, and 45-60 after implantation. Group II rabbits were intramuscularly injected with 10 μg/kg dalargin, a growth stimulator [4], immediately after implantation and then daily during 4 days. Morphometric parameters of the microvessels, the degree of vascularization and the mean diameter and length of microvessels in the field of view were measured using a Leitz-Tas image analyzer [6]. The significance of changes in these parameters during revascularization was evaluated using the Student's *t* test.

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## RESULTS

The dynamics of the morphometric parameters of MCB during 10 days after the appearance of first microvessels and 2-3 months after implantation of the chambers is shown in Fig. 1. Comparison of curves *1* (Fig. 1, *a*, *b*) revealed a high density of vascularization in the left ear (LE) practically at the beginning of monitoring. The area of vascularization and the length and diameter of vessels slightly varied over the observation period (within 18, 16, and 6%, respectively). In vertebrates, the regression of blood vessels, a component of vascular bed formation, is

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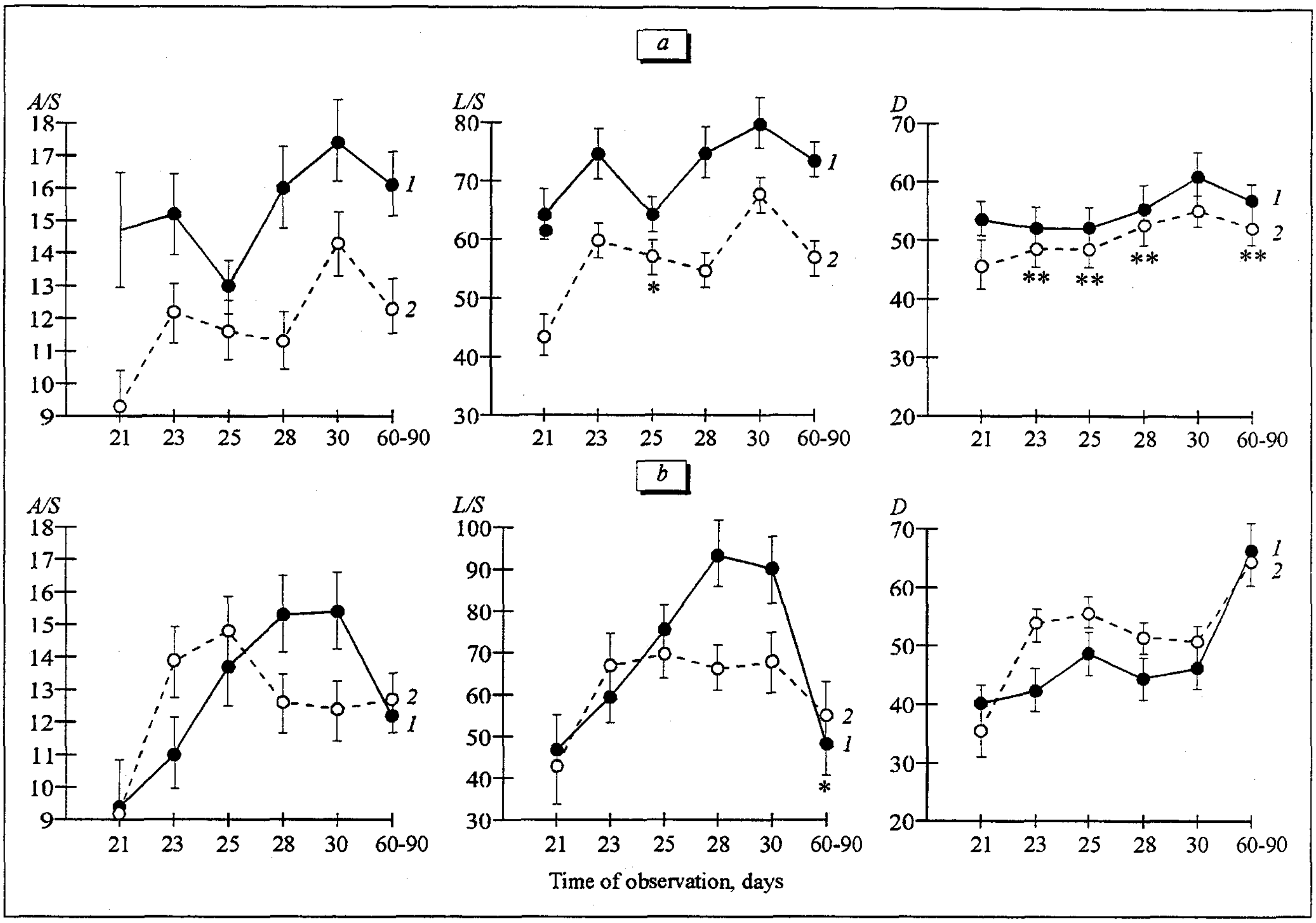


**Fig. 1.** Area of vascularization, length and mean diameter of regenerating microvessels in left (*a*) and right (*b*) ears of animals treated (*2*) and nontreated (*1*) with dalargin. Ordinate: area of vascularization, *A/S* (%); relative length of microvessels, *L/S* ($mm/cm^2$); mean diameter of microvessels, *D* (μ). *Differences from the first day of observation are statistically insignificant; **differences between curves *1* and *2* are statistically insignificant. For other values $p<0.05$.

slightly pronounced during embryogenesis of the left body side [5]. By contrast, the curves reflecting the formation of MCB in the right ear (RE) have the shape of a parabola. At the beginning of monitoring, the area of vascularization in the RE was 60% lower than in the LE, and the length and diameter of blood vessels were lower than in the LE by 36 and 35%, respectively. On days 28-30, we observed excessive vascularization which decreased to the end of observation period. A similar dynamics was observed in healing of a tissue lesion, when excessive vascularization observed on day 9 then returned to normal [3]. Since the degree of vascularization depends on the diameter and total length of microvessels, it should be noted that the excessive vascularization in RE is normalized through reduction in the number of perfused vessels, whereas their mean diameter increased.

Curves *2* on the figure represent the dynamics of morphometric parameters of MCB in the ears of dalargin-treated rabbits. Comparison of curves *1* and *2* (Fig. 1, *a*, *b*), shown that dalargin exerts different effects on microvessels in LE and RE. The drug inhibits vascularization in LE, especially at the beginning of the observation period (by 58%) primarily due to reduction in the number of perfused vessels, while in RE it shifts the phase of excessive vascularization, thus accelerating regeneration. The total length of microvessels decreases similarly to that in LE, while the shape of the regeneration curve is preserved due to a rise of the mean diameter of microvessels. The dynamics of vascularization area is similar to that of the diameter of microvessels in RE and their total length in LE. Concerning the MCB parameters on the first day of the observation period, it should be noted that dalargin suppresses regeneration in the early period (before day 21), the effect being more pronounced in LE. However, the rate of vascularization increases. This indicates that when used as a therapeutic means, dalargin should be administered at different times in right- and left-side injuries. In the left-side injuries, a delayed application of dalargin is probably more effective (its inhibiting effect on vascularization at the early stages of regeneration is diminished), while in right-side injuries the drug should be applied as described above.

Our findings suggest that the principle of left-to-right gradient maturation established for the functions of contralateral regions in the brain is also valid for regeneration of the microcirculatory bed in peripheral paired organs and results in a more rapid vascularization of the left-sided organ. Moreover, any intervention into regenerative or pathological processes in microvessels is more effective when location of the injury is taken into account [5].

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# Serotonin-Producing Cells in the Duodenum of Hibernants During Periods of Hypothermia in Midwinter and Before Awakening in the Spring

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Ultrastructural differences are demonstrated between the duodenal serotonin-producing cells of ground squirrel during periods of hypothermia in winter and before awakening in the spring. In spring, the free ribosomes/polysomes ratio changes in these cells, and serotonin is actively released from secretory granules. These changes are associated with the preparation of the digestive system to functioning after hibernation.

**Key Words:** *hibernation; hypothermia; hibernant; enterochromaffin cells; serotonin*

Duodenal serotonin-producing (EC) cells of the hibernants differ substantially in ultrastructure during normo- and hypothermia, i.e., in summer and winter [4]. These seasonal differences are due to those in their functional significance in different periods of the year. In summer, the secretory product accumulates in these cells, where it is stored as cytoplasmic granules and utilized for regulation of the digestive tract activity. In fall and winter, the major ingredient of secretory granules, serotonin, becomes necessary for hibernation [2].

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In this study we examined duodenal serotonin-producing cells of ground squirrels during two different periods of hibernation, namely, in the middle of winter and before awakening in the spring, in order to reveal possible reorganizations in these cells before the active period of life begins.

## MATERIALS AND METHODS

The objects of the study were red-cheek ground squirrels (*Citellus erythogenys* Brandt) living in Western Siberian steppes. They begin to hibernate late in September and come out of hibernation in April. The hibernation is cyclic, with periods of hypothermia interrupted by spontaneous awakenings, when the body temperature progressively rises to normal before de-

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