INFLUENCE OF VITAMINS B_6 AND B_{12} ON POSTNATAL VASCULAR DEVELOPMENT IN THE ANIMAL BRAIN

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The multiplication of capillaries by budding, which continues for some time after birth in the brains of man and animals in which development is incomplete at the time of birth, may be affected by a number of factors (asphyxia, cerebral trauma, hydrocephalus, etc.) [1, 2]. There has been little or no investigation on the effects of pharmaceutic preparations on development in the cerebral vascular system.

It was therefore decided to examine the effects of vitamins B_6 and B_{12}, which are in wide clinical use and are of considerable importance for the correct development and functioning of the nervous system, on capillary multiplication and, consequently, the density of the capillary network in the animal brain.

METHOD

The experimental animals were albino rats, 7-8 days old, an age at which there is active growth of capillaries in the brain. The control group consisted of 32 animals; 23 rats were given subcutaneous injections of vitamin B_6 (0.02 mg / 10 g body weight) every second day, and 29 rats, similar injections of B_{12} (0.4 mg/10 g). The preparations were injected in 0.1 ml 0.5 percent novocain. The dose selected may be regarded as equivalent to average therapeutic doses. Some of the control rats received injections of 0.1 ml 0.5 percent novocain over the same period.

Most of the rats were decapitated at the age of 16, 18 or 19 days, by which time they had received 4 or 5 vitamin injections. The brains were fixed in 10 percent formalin; after impregnation of the vascular network in the brain by the Klosovskii method [2], preparations were made and counts were made of growing capillaries in cerebral cortex (frontal, parietal and occipital regions), medulla and cerebellar hemispheres. The remaining animals were killed when they reached the age of 30 days, after 10-12 vitamin injections. The vascular system of the brains of these rats was filled with Indian ink (3 percent solution of gelatin in Indian ink) for calculation of the density of the capillary network in three or four layers of the cerebral cortex and in the medulla (with a magnification of 400 ×). The density or total length of the capillary network was expressed in mm/mm^3.

RESULTS

The vitamins administered did not have any very significant effect on the animals' general development. The only difference was that the brains of the rats given vitamin B_{12} tended to be slightly heavier and larger, with possibly a larger number of lamellae in the vermis of the cerebellum. The eyes of the rats given vitamin B_6 opened a day earlier than those of the control animals, and these animals exhibited greater excitability and motor activity.

The counts of growing capillaries in the brains of experimental and control animals are given in Table 1.

In the 16-day old control animals the largest numbers of growing capillaries were found in the reticular formation of the medulla and then in the various cortical regions; there were still less in the cerebellar hemispheres. There was a definite relationship between the various stages of the growing capillaries in all areas: hydroid stages were more than three times as numerous as bud and polyp stages. Capillaries could be observed growing from large vessels and there were some "double " growing capillaries.

TABLE 1. Changes in the Numbers of Growing Capillaries in the Brains of Rats Given Vitamin B_6 and Vitamin B_{12} (100 fields)

Age of rats (days)	Group	Average number of capillaries seen with magnification of 400 × (M ± m)				
		Cerebral cortex				
		Frontal	Parietal	Occipital	Cerebellar hemispheres	Medulla
16	Control	127 ± 6.27	102 ± 14.98	123 ± 2.41	72 ± 12.64	185 ± 20.36
	Vitamin B_6	66 ± 2.69	59 ± 5.15	67 ± 10.51	56 ± 5.44	88 ± 4.80
	Vitamin B_{12}	76 ± 15,64	47 ± 10.59	62 ± 7.55	66 ± 22.72	103 ± 31.4
18	Control	81 ± 13.78	72 ± 6.56	82 ± 11.27	23	59
	Vitamin B_6	40 ± 4.62	55 ± 7.75	46 ± 2.47	—	—
	Vitamin B_{12}	72 ± 7.51	70 ± 8.76	85 ± 10.76	—	—
19	Control	26 ± 4.41	29 ± 3.87	22 ± 2.64	11 ± 1.77	16 ± 2.14
	Vitamin B_6	30 ± 4.65	27 ± 7.11	24 ± 1.67	—	—
	Vitamin B_{12}	33 ± 6.65	40 ± 15.75	31 ± 6.11	44 ± 3.46	106 ± 21.40

TABLE 2. Changes in Density of Capillary Network in Cerebral Hemispheres and Medulla of 30-Day Old Rats Given Vitamin B_6 and Vitamin B_{12} (mm/ mm^3 tissue)

Group	Mean density of capillary network (M + m)			
	Cerebral cortex			
	Frontal	Parietal	Occipital	Medulla
Control	1203 ± 56.64	1257 ± 77.33	1229 ± 67.19	1048 ± 57.77
Novocain				
Vitamin B_6	1305 ± 100.06	1371 ± 59.35	1171 ± 42.52	—
Vitamin B_{12}	1442 ± 37.04	1305 ± 52.43	1171 ± 18.41	—
	1583 ± 33.10	1451 ± 117.29	1251 ± 48.37	1808 ± 87.86

In the 18- and 19-day old rats capillary development was much less intense in all parts of the brain. The largest numbers were found in the cerebral cortex. There were fewer capillaries growing from large vessels than in the 16-day rats.

When novocain was injected, newly formed capillaries in the frontal cortex appeared to be more numerous than in controls. The density of the capillary network in the cortex of frontal and parietal regions was 8-9 percent greater than in the control animals but the density of the network in the occipital cortex was somewhat less (Table 2). Statistically, however, these differences were not significant.

When the rats were given vitamin B_6 between the ages of 7 and 16-18 days, the capillary count was reduced by 25-50 percent in all parts of the brain (see Table 1). The number of growing capillaries seen on the 19th day was higher again, values being more or less at control level. Vitamin B_6 also appeared to produce a general dilatation of vessels and capillaries in all parts of the brain. On the 30th day there was some increase in the density of the capillary network in the cortex of the frontal region but no further changes elsewhere. The difference in the values for the frontal region between experimental and control animals was 10-11 percent and statistically significant (see Table 2).

There was considerable reduction of the rate of capillary multiplication in 16-day rats which had been given vitamin B_{12}; the reduction (25-50%) was observed in all parts of the brain, but was least in the cerebellar hemispheres. The number of growing capillaries had increased to control values by the 18th day and was 50% above the latter on the 19th, the increase being particularly evident in medulla and cerebellum.

When vitamins B_6 and B_{12} were administered together, the relative numbers of capillaries in the different stages of growth were much the same as in control animals. Some double capillaries growing from large vessels were observed.

The density of the capillary network in 30-day old rats given vitamin B_{12} exceeded the control density by 21% in the frontal cortex, 6% in parietal and occipital cortex and 17.5% in the medulla. The increases were significant in the case of frontal cortex and medulla.

The administration of vitamins B_6 and B_{12} to growing animals thus affected the process of capillary multiplication and the density of the capillary network in several parts of the brain. Neither vitamin had any pathological effect on these processes.

LITERATURE CITED

1. T. P. Zhukova, Byull. Éksp. Biol. No. 6, p. 87 (1961).
2. B. N. Klosovskii, The Cerebral Circulation (Moscow, 1951).

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
