

EFFECT OF VITAMIN A DEFICIENCY ON BLOOD  
CONCENTRATIONS OF FOLIC AND FOLINIC ACIDS  
IN *Macacus rhesus*

Z. N. Dzhelieva, A. V. Trufanov,  
and V. A. Karpacheva

UDC 616.391.04:577.161.11-092.9-07:  
616.153:577.164.17-074

Too little is known about the relationship between the metabolism of vitamin A and folic acid in the animal organism. The study of this problem is important for enabling the correct dosage of vitamins to be given in health and disease.

In the present investigation the blood levels of folic and folinic acids were studied in monkeys with avitaminosis A.

EXPERIMENTAL METHOD

Experiments were carried out on 8 rhesus monkeys of both sexes aged 3.5 years and weighing 2-3 kg.

All the monkeys at first were kept on a balanced synthetic diet, after which they were transferred to a diet of the following composition: 76% polished rice, 6% corn oil, 15% casein purified from vitamins [5], 3% salt mixture, and a mixture of vitamins [6].

The vitamin mixture was administered through a tube twice a week [3]. The daily dose of folic acid was 0.5 mg. No vitamin B<sub>12</sub> was administered.

Experiments were carried out on three groups of monkeys. Group 1 consisted of three animals not receiving vitamin A, group 2 of three monkeys receiving vitamin A in a daily dose of 30 µg, and group 3 of two monkeys receiving 45 µg vitamin A daily.

Observations were made before and during the 4 months after the animals had been transferred to the vitamin A deficient diet. The criteria of vitamin A deficiency were the content of vitamin A in the liver, changes in the cornea, and the general clinical condition.

The vitamin A content in the liver was determined in punch biopsy material [2] and the concentrations of folic and folinic acids were determined in whole blood by a microbiological method based on stimulation of growth of *Streptococcus faecalis* R. and *Pediococcus cerevisiae*. The principal and maintenance media were prepared as described by Herbert [4]. The whole blood was treated by Toennies' method [7].

EXPERIMENTAL RESULTS

A decrease in the vitamin A content in the liver was observed in the monkeys not receiving vitamin A and receiving vitamin A in a dose of 30 µg. In the animals receiving 45 µg vitamin A, no decrease in the vitamin A content in the liver was observed (Table 1).

Clinical manifestations of vitamin A deficiency were observed in two monkeys of group 2, receiving 30 µg vitamin A, and in all the monkeys of group 1, not receiving vitamin A. These manifestations took the form of clouding of the cornea, anorexia, loss of weight, and increased susceptibility to infection. Monkey No. 3 from group 1, for example, developed a relapse of dysentery caused by *Shigella flexneri*, leading to death of the animal two months after the beginning of administration of the vitamin A deficient diet. The vitamin A content of the liver of this monkey was only 6.8 µg/g. Another monkey (No. 1) of this

---

Institute of Experimental Pathology and Therapy, Academy of Medical Sciences of the USSR, Sukhumi (Presented by Active Member of the Academy of Medical Sciences of the USSR B. A. Lavrov). Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 64, No. 8, pp. 48-50, August, 1967. Original article submitted March 4, 1966.

TABLE 1. Vitamin A Content in Liver of Monkeys Receiving a Diet without the Vitamin

Group of monkeys	Daily dose of vitamin A (in $\mu$ g)	Monkey No.	Vitamin content in liver ( $\mu$ g/g liver)			Clinical state of monkey after four months
			Back-ground	After two months	After four months	
1	0	1	55.5	12.7	9.2	Adynamic. Poor appetite, clouding of the cornea
		2	34.0	12.3	11.8	The same. Sensitivity of cornea lowered
		3	17.2	6.8	—	Diarrhea, blood-stained stools Sensitivity of cornea lowered
2	30	1	33.0	20.1	19.7	Polyneuritic syndrome. Diarrhea, clouding of the cornea
		2	30.9	26.0	23.0	Healthy
		3	39.2	23.6	21.0	Polyneuritic syndrome Clouding of the cornea
3	45	1	58.2	46.3	71.0	Healthy
		2	49.6	50.8	53.5	Healthy

TABLE 2. Blood Concentration of Folic and Folinic Acids in Monkeys Developing Avitaminosis A

Group of monkeys	Daily dose of vitamin A (in $\mu$ g)	Monkey No.	Blood concentration of folic and folinic acids (in $m\mu$ /ml blood)							
			Background*		After two months		After three months		After four months	
			Folic acid	Folinic acid	Folic acid	Folinic acid	Folic acid	Folinic acid	Folic acid	Folinic acid
1	0	1	8.1	4.2	4.0	2.0	0.6	0.0	—	—
		2	10.0	4.6	5.8	2.1	1.6	0.3	1.2	0.8
		3	11.7	4.2	6.2	1.8	—	—	—	—
2	30	1	7.5	5.7	5.0	3.9	2.3	2.0	1.9	1.5
		2	7.4	5.2	7.0	4.8	2.3	2.6	2.3	1.9
		3	4.7	2.5	4.8	1.4	1.3	0.3	1.5	0.8
3	45	1	4.0	3.4	3.4	2.0	4.8	2.6	5.5	1.8
		2	3.7	3.2	4.0	2.8	4.0	3.0	5.7	4.2

\*Mean of two determinations.

same group died four months later with signs of vitamin A deficiency and a fall in the vitamin A content of the liver to 9.2  $\mu$ g/g.

It is clear from Table 2 that as the monkeys not receiving vitamin A developed avitaminosis A, their blood levels of folic and, in particular, folinic acid fell sharply.

In the monkeys receiving 30  $\mu$ g vitamin A daily, a marked fall in the blood levels of folic and folinic acids was also observed, but it was not so severe as in the monkeys of group 1.

In the monkeys of group 3, receiving 45  $\mu$ g vitamin A daily, maintaining them in a normal physiological condition, no changes were found in the folic and folinic acid concentrations.

The mechanism of the changes in the blood levels of folic and folinic acid in monkeys with vitamin A deficiency is not clear. These vitamins, however, are known to participate in regenerative processes in the body. In vitamin A deficiency regeneration of the epithelium covering various organs is considerably affected. Folic and folinic acids are directly related to regeneration of the intestinal epithelium [1].

In vitamin A deficiency the body evidently requires large amounts of folic and folinic acids, leading to exhaustion of their reserves. This was seen particularly clearly in the monkeys with diarrhea, modifying the biosynthesis of folic and acid in the intestine and increasing its elimination from the body.

It follows from these observations that in vitamin A deficiency in monkeys conditions are created in the body contributing to a reduction in the concentration of folic and folinic acids in the blood.

#### LITERATURE CITED

1. N. P. Bochkov, Z. N. Dzhelieva, M. I. Kuksova, et al., in the book: Problems in the Physiology and Pathology of Monkeys [in Russian], 235, Sukhumi (1961).
2. V. A. Karpacheva, Byull. éksp. Biol., No. 6, 118 (1965).
3. S. N. Matsko and A. T. Zhmeido, Doklady Akad. Nauk SSSR, 106, No. 2, 367 (1956).
4. V. Herbert, R. Fisher and B. Koontz, J. Clin. Invest., 40, 81 (1961).
5. P. Malathi, K. Subba Rao. P. Sachadri Sastry, et al., Biochem. J., 87, 305 (1963).
6. V. Ramalingswany, E. H. Leach, S. Sreramachari, J. Quart. Exp. Physiol., 45, 337 (1960).
7. G. Toennies, E. Usdin, and Ph. Phillips, J. Biol. Chem., 221, 855 (1956).