# EFFECT OF LARGE DOSES OF VITAMIN $D_2$ ON ERYTHROPOIESIS

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Vitamin $D_2$ in a dose of 150,000 i.u./kg body weight daily inhibited regeneration of the erythrocytes after intensive blood loss in rats. Some degree of slowing of the blood regeneration process also took place after administration of 15,000 i.u./kg body weight vitamin $D_2$. The accompanying administration of vitamin $B_{12}$ did not prevent the action of vitamin $D_2$ on erythropoiesis.

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Administration of large doses of vitamin D for the prevention and treatment of rickets [8, 12] and for the treatment of tuberculosis of the skin [7] and carcinoma of the lung and lymphogranulomatosis [10] in some cases causes hypervitaminosis D. The clinical picture of hypervitaminosis D is characterized by disturbances affecting the kidneys and cardiovascular system, resulting from pathological calcification of the renal tubules and arterial walls [12, 14]. Some workers have observed hypochromic anemia in patients with vitamin D poisoning [1, 4, 5]. These observations suggest that vitamin D in large doses may inhibit erythropoiesis.

In the present investigation the action of various doses of vitamin $D_2$ on regeneration of the erythrocytes after acute blood loss was studied in rats.

## EXPERIMENTAL METHOD

Experiments were carried out on male rats with a mean weight of 300 g. The animals were divided into three groups of 7 rats in each group. Daily for 21 days the rats received an oily solution of vitamin $D_2$ by mouth: in group 1 in a daily dose of 150,000 i.u./kg (3.75 mg), and in group 2 15,000 i.u./kg. Control animals received the corresponding volume of vegetable oil. On the 8th day after the beginning of administration of the vitamin 2 ml blood was taken from the tail vein of all the animals.

The erythrocytes and reticulocyte counts in the blood were determined before bleeding and on the 2nd, 4th, 6th, and 10th day thereafter. Erythrocytes were counted in a Goryaev's chamber and reticulocytes were stained by Alekseev's method and counted in films.

## EXPERIMENTAL RESULTS

As Fig. 1 shows, bleeding led to a considerable decrease in the erythrocyte count in all groups. From the 4th day after bleeding the erythrocyte count in the control group began to rise gradually and on the 10th day it had almost regained its original level. In the animals of group 2, receiving small doses of vitamin $D_2$, the erythrocyte count also rose but not so rapidly as in the control. In the animals of group 1, receiving large doses of vitamin $D_2$, the erythrocyte count remained at the same level, i.e., the lost blood was not made good.

Reticulocyte counts (Fig. 2) showed that in the control animals a typical reticulocyte wave took place after blood loss with a maximum increase on the 4th day when the reticulocyte count reached 11%. In the animals of group 2, receiving small doses of vitamin $D_2$, the number of reticulocytes also increased after blood loss, although less intensively. In the rats of group 1, receiving large doses of vitamin $D_2$, the reticulocyte wave was completely absent. In some animals of this group no reticulocytes whatever could be found in the films.

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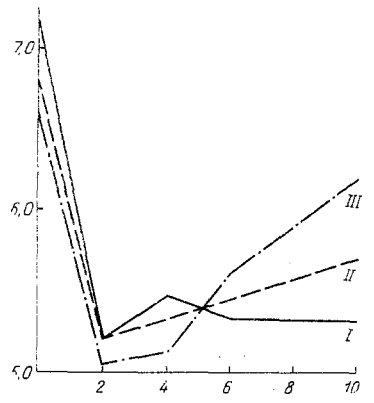


Fig. 1. Erythrocyte count after blood loss under normal conditions and in hypervitaminosis D. I) Animals receiving 150,000 i.u./kg vitamin $D_2$ daily; II) animals receiving 15,000 i.u./kg vitamin $D_2$ daily; III) control group. Ordinate, erythrocyte count (in millions); abscissa, days after blood loss.

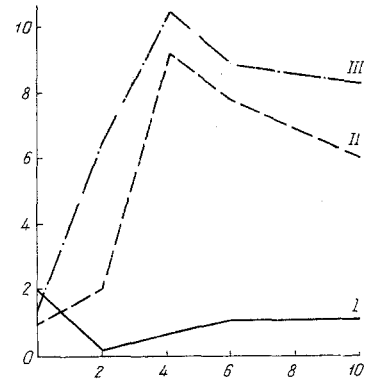


Fig. 2. Reticulocyte count after blood loss under normal conditions and in hypervitaminosis D. Significance of curves as in Fig. 1. Ordinate, reticulocyte count (in percent), abscissa, days after blood loss.

The results thus show that vitamin $D_2$ in a dose of 15,000 i.u./kg (0.375 mg) slightly inhibits the erythropoietic function of the bone marrow, but in a dose of 150,000 i.u./kg (3.75 mg/kg) it practically completely suppresses erythropoietic function.

Because of the role of vitamin $B_{12}$ in hematopoiesis, an attempt was made to determine whether this vitamin can prevent or reduce the inhibitory action of vitamin $D_2$ on bone marrow function. For this purpose 2 further groups of animals were included in the experiments and these received vitamin $B_{12}$ intramuscularly in a dose of 20 $\mu$g per rat on alternate days in addition to vitamin $D_2$. This investigation showed that vitamin $B_{12}$ had no protective effect: the inhibitory action of both large and small doses of vitamin $D_2$ was just as intensive in the animals receiving vitamin $B_{12}$ as in those not receiving it.

The results indicating the action of large doses of vitamin $D_2$ on erythropoiesis should be compared with those obtained by other workers [13] who found that vitamin $D_2$ in doses of 360,000-750,000 i.u./kg inhibits regeneration of the rat liver after partial hepatectomy. Taken as a whole, these results provide evidence that vitamin $D_2$ is able to inhibit regeneration and growth of various tissues. Possibly these cytostatic properties of vitamin D may account for the beneficial effect of its administration in the treatment of malignant neoplasma [10].

The inhibitory action of vitamin D on tissue regeneration and growth may be connected with disturbances in metabolism arising after administration of large doses of this vitamin. It was previously shown that vitamin $D_2$ in several tissues inhibits adenosine triphosphatase activity [6, 8] in several tissues and dissociates oxidative phosphorylation [11]. The inhibitory action of vitamin $D_2$ on tissue growth may also be due to the formation of peroxides from it, causing oxidation of cytochrome C [2] and destruction of the lipoprotein membranes of cells and subcellular structures [3].

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