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Effect of Cobalt on Erythropoiesis in Anemic Rabbits.

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During the past few years, in our experiments with different types of erythropoietic stimuli, the effect of cobalt on red cell formation appeared most impressive. Even such potent stimuli as excessive bleedings, or low oxygen tensions, do not evoke or maintain as great a reticulocyte response as does the injection of cobalt. It seemed advisable, therefore, to test the influence of cobalt on certain types of anemia.

In this report we shall describe the effects of cobalt on recovery from two types of artificially induced anemias in rabbits. One type was brought about by repeated bleedings and the other by injections of benzol. All animals were fed a normal diet consisting largely of Purina chow, lettuce and carrots throughout the entire experimental period.

In the first series of experiments 10 rabbits were bled approximately one-third of their calculated blood volumes on 3 occasions over a period of 2 weeks. This resulted in a fall of red cell count from 6.0-6.5 million per mm^3 to 2.5-3.1 million per mm^3. Corresponding to this drop in red cell count, the reticulocytes showed a sharp rise to 15-22%. On the third day following the reticulocyte peak, the animals were divided into 2 groups. Five animals were allowed to continue untreated, whereas the other 5 were injected daily with 50 mg $Co(NO_3)_2.6H_2O$. In the untreated group the reticulocytes disappeared from the circulating blood quite rapidly and reached normal values approximately 25 days later. The normal red cell count in these animals was attained in about 25-30 days. The anemic animals treated with cobalt, however, showed a marked reticulocyte response which was maintained at values of 8-10% or higher throughout the experimental period. The red cell counts in these cobalt-treated animals reached normal levels in about 15 days and continued to rise, reaching a value of 7.0-7.8 million per mm^3 10 days later.

In the second series, 12 rabbits were injected daily, for approximately 5 weeks, with gradually increasing amounts of benzol ranging from 0.5-1.0 cc. At the end of this period of treatment the red cell

count had dropped from 6.0-6.6 to 3.5-4.5 million per mm^3. The reticulocyte percentage decreased to a significant extent, and the white cell counts were extremely low. From this time on, all the animals continued to receive daily injections of one cc benzol, but half of these, in addition, were injected daily with 50 mg $Co(NO_3)_2.6H_2O$. In the animals treated with benzol alone, the red cell count continued to drop, reaching a value of 2.5-3.8 million per mm^3 at the end of 50 days of treatment. Further injections of benzol into such animals generally resulted in death. In the animals receiving cobalt in addition to the benzol, the reticulocytes rose sharply from 0.5-1.2% to 10.4-13.8% within 2 weeks. This rise of reticulocytes was soon accompanied by an increase in the red cell count which attained almost normal levels at the end of 4 weeks.

In contrast to the severely hypoplastic condition of the benzol-treated animals' marrows, the marrows of cobalt-benzol injected rabbits showed marked hyperplasia, even greater than that observed in normal animals.

The marrows of normal rabbits treated with cobalt for 45 days show large numbers of megakaryocyte-like cells which appear to give rise to clusters of erythrogenic cells, in a manner comparable to that described by Jordan[1] in the yolk sac of the pig and in marrow of humans afflicted with typhoid. This would involve the formation of giant hemogenic cells or polykaryocytes from megakaryocytic elements by a direct division of the polymorphous nucleus. In the benzol-treated animals, where hemocytoblast development is inhibited, cobalt was found to markedly stimulate mitosis of the erythroblast and normoblast elements.

Summary. Cobalt injected into animals subjected to repeated bleedings or treated with benzol results in a rapid recovery from the anemia. Cobalt produces this effect by stimulating the formation of erythrogenic precursors in the bone marrow.

[1] Jordan, Harvey E., *Am. J. Anat.*, 1918, **24**, 225.