

## 91. COMPARISON OF EFFECTS OF FOLIC ACID AND FOLINIC ACID IN EXPERIMENTAL MEGALOBLASTIC ANEMIA

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Some of the chemical properties and effects on the growth of microorganisms of a substance termed *citrovorum* factor or folinic acid have been reported. We have tested the effect of a synthetic preparation of folinic acid on blood formation in experimentally produced megaloblastic anemia. This megaloblastic anemia was produced in monkeys accompanying a deficiency of ascorbic acid in a manner similar to that previously described. The megaloblastic anemia so produced has a marrow pattern nearly identical with that seen in megaloblastic anemia in human beings.

Monkeys weighing approximately 2 kg., which had well-marked megaloblastic patterns in the marrows, and were quite comparable, were treated with intramuscular injections as follows:

No. 24—15 mg. folic acid

No. 50—50 micrograms crude folinic acid (15 per cent folinic acid)

No. 51—100 micrograms crude folinic acid (30 per cent folinic acid)

No ascorbic acid was given the animals which were scorbutic as well as megaloblastic.

The effects of the small doses of folinic acid were as prompt and complete as that produced by the much larger dose of folic acid. In each case the megaloblasts disappeared from the marrow within forty-eight hours; after ten days the marrows were essentially normal. The responses in the peripheral bloods demonstrated equivalent and convincing effects as regards reticulocytosis, increase in hemoglobin, erythrocytes, and leucocytes. Detailed hematologic data will be presented.

Fifty micrograms of folic acid intramuscularly daily in a similar animal produced no significant effect on the marrow within forty-eight hours; a 750 microgram dose of folic acid intramuscularly in another monkey had less effect on the megaloblastic marrow than the 50 microgram dose of crude folinic acid.

The striking effect on the megaloblastic marrow produced by as little as the 7.5 micrograms of folinic acid contained in one of the preparations is particularly interesting, considering the animals were scorbutic. Ascorbic acid was not necessary for the action of folinic acid. It would appear folinic acid

is considerably more effective than folic acid in experimental megaloblastic anemia. This lends support to the concept that folic acid exerts its hemato-poietic effect through conversion into a more active derivative such as folinic acid.