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ABSTRACTS—Concluded

61. EXPERIMENTAL PRODUCTION OF MEGALOBLASTIC ANEMIA; AN INTERRELATIONSHIP BETWEEN ASCORBIC ACID AND PTEROYLGLUTAMIC ACID

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This report describes a means of producing megaloblastic and macronormoblastic anemia in monkeys using deficient diets alone.

The diets employed were basically dried cow's milk reconstituted with water and adjusted with lactose and vegetable oils and supplemented with crystalline vitamins to provide liquid diets of the following approximate composition:

	PER 100	ML.
Protein	1.6	Gm.
Carbohydrate	7.2	Gm.
Fat	3.3	Gm.
Calories	67	
Vitamin A	800	I. U.
Vitamin D	50	I. U.
Thiamin	.07	mg.
Riboflavin	.1	mg.
Nicotinic acid	.5	mg.

Any other vitamins present were those contained in the milk. Each experimental animal was given .137 mg. Fe per kilogram in the form of iron ascorbate intravenously at the start of the experiment followed by several weeks of oral therapy with 4 c.c. of ferrous gluconate daily.

In five control periods monkeys fed this type of diet ad libitum and 50 mg. ascorbic acid daily for five or more months remained in good health and did not develop anemia or changes in the bone marrow.

When the experimental diet was fed to eleven monkeys without the addition of ascorbic acid, a typical sequence of events occurred. For three to four months they remained in apparent good health. At about this time the first symptoms of scurvy appeared. They remained essentially in this state for the next three to four weeks, exhibiting only the symptoms of scurvy, without developing anemia or definitive changes in the marrow. Then a precipitous deterioration began. Pronounced anorexia and listlessness ushered in this phase. Diarrhea commenced invariably, the stools being loose to mushy, bulky, and foul but without pus or blood. With one exception a histamine refractory gastric achlorhydria developed. The fur lost its smoothness and luster and was shed in large amounts. The peridontal gingivae became ulcerated and necrotic. No changes were seen in the tongue. No infections were observed in the animals at any time. Anemia and neutropenia developed rapidly without evidence of additional hemorrhage. The anemia was usually of a normocytic or macrocytic type.

The most critical criteria were applied in designating the types of cells seen in the marrow. Three monkeys developed megaloblastic marrows very similar to, if not identical with, those seen in megaloblastic anemia in human

beings. The marrows in the other eight animals became macronormoblastic, a stage through which the megaloblastic marrows passed. The alterations in the granulocytes in each instance were striking, showing hypersegmentation and large early forms with premature lobulation such as are seen in the marrow in pernicious anemia. It was the impression that all the marrows might have progressed to a frankly megaloblastic picture if the precarious condition of the animals had not made it seem necessary to treat them in order to test the effects of various agents.

A systematic trial of vitamin B₁₂, PGA, and ascorbic acid revealed the following: (1) Ascorbic acid given relatively early in the disease gradually restored the animal to health and the marrow and blood became normal. (2) If ascorbic acid was not given until an advanced stage of the disease, it did not restore the marrow to normal or prevent the death of the animal. (3) Vitamin B₁₂ alone, given intramuscularly, had no effect on the marrow within forty-eight hours. (4) PGA, given orally or intramuscularly as the free acid or the triglutamate, but without ascorbic acid, promptly stimulated normal hematopoiesis in the marrow and relieved all the symptoms not attributable to scurvy. When ascorbic acid was added, normal health was restored even though the experimental diets were continued.

Increasing the protein in the diet to 3.3 Gm. per 100 c.c. by adding calcium caseinate did not prevent the development of the characteristic anemia.

Thus it would appear that megaloblastic anemia developed as a result of PGA deficiency somehow induced by a chronic deficiency of ascorbic acid.

62. CERTAIN EFFECTS OF CHEMOTHERAPY ON THE FECAL AEROBIC AND ANAEROBIC BACTERIA OF PATIENTS WITH CHRONIC ULCERATIVE COLITIS

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The role of the fecal bacteria in the pathogenesis and course of chronic nonspecific ulcerative colitis is not clear. A method of simplifying the bacterial flora of the feces and reducing the number of bacteria in the bowel would provide useful information concerning this problem. Accordingly, qualitative and quantitative studies of the aerobic and anaerobic bacteria were made before and after treatment with absorbable and nonabsorbable sulfonamides, penicillin administered orally and parenterally, and the oral administration of streptomycin, aureomycin, and chloromycetin. Control studies consisted in observations intended to determine the error of the method and to ascertain the spontaneous day-to-day variation. The drugs were administered for relatively long periods of time; bacteriologic studies were carried out at frequent intervals in order to determine the initial and late effects of chemotherapy. All of the drugs, under certain conditions, are capable of altering the aerobic flora; some also may modify the anaerobic flora of the feces, the degree and duration of effect varying considerably. For instance, sulfonamides alter the aerobic flora, when initially used, for periods as long as six weeks. Streptomycin, on the other hand, exerts a marked quantitative effect, which is maintained, however, only for several days. Chloromycetin and aureomycin exert an intermediate effect: the *B. coli* disappear and the total bacterial count initially falls and then rises, with the reappearance of *B. coli* as a predominant organism. In addition, after the initial depression of bacterial counts had terminated, the counts tended to rise above the control levels and to remain high, decreasing to control levels only after the drugs were discontinued.