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Production in Dogs of a Syndrome Similar to Sprue by Diets Deficient in Vitamin B_2.

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The value of the vitamin B complex in the therapy of sprue in Porto Rico has been established.[1] In cases of severe anemia its oral administration effected reticulocyte rises and improvement of blood values. In other cases presenting glossitis and diarrhea without severe anemia, the symptoms were promptly and completely relieved. These observations suggested that lack of vitamin B might be an important factor in the etiology of sprue. Accordingly, experiments with 50 dogs have been carried out to ascertain the effect of prolonged feeding of diets partially but not completely deficient in vitamin B_2.

The animals used were as old and as large as could be obtained. They were kept under uniform conditions. The diet fed was a modification of the Goldberger "black tongue producing" diet. It was low in protein, high in fat and carbohydrate, and contained only the vitamin B present in rice polishings. It contained the following ingredients:

	gm.		gm.
White corn meal	4,000	Cotton seed oil	300
Ground California black-eyed peas	500	Cod liver oil	200
Washed casein	500	Salt mixture (Cowgill)	50
Sugar	300	Rice polishings	400

The corn meal, peas and casein were thoroughly mixed and cooked 2 hours in a steam cooker. The sugar, oil, rice polishings, and salt mixture were then added. This amount was given daily to 40 dogs. The animals were allowed as much of the diet as they would take.

Careful studies of the blood were made at regular intervals. A certain number of the dogs fed the diet deficient in vitamin B_2 acquired a condition similar in some respects to sprue in human beings. The remainder developed a syndrome to be described later. Stomatitis was present in a mild degree in all. The buccal mucous membrane was injected and contained a variable number of circumscribed yellowish aphthae. Glossitis was a marked feature. In the

[1] Castle, W. B., and Rhoads, C. P., *Lancet*, 1932, **1**, 1198.

earliest stages atrophy of the papillae of the tip and sides of the tongue occurred, leaving a smooth, deep pink to red surface. As the condition progressed the color became a deeper red to a fiery scarlet. The atrophic process extended dorsally and medially until, in certain animals, only a few papillae remained at the base of the tongue.

Gastro-intestinal disturbance was marked. At the height of the glossitis many animals partly or completely refused food of any kind. Vomiting was frequent and occasionally severe. Chronic diarrhea was a striking feature. The stools were sometimes watery but more often yellow, voluminous and semi-solid in consistence.

All of the animals lost weight and in many cases to such a degree that they became emaciated. The average loss in this series was 4.51 kilos or 24% of the weight at the beginning of the experiment.

The blood changes were definite in 60% of the animals and striking in 30%. The average red cell count of the latter group at the beginning of the experiment was 6.44 millions. At the low point of the anemia it was 3.105 millions. There was an average decrease of 3.337 millions or over 50%. The average hemoglobin value as done by the Sahli acid hematin method, using calibrated tubes and standards, was 87.7% at the outset and 56.4% at the low point. The average decrease of hemoglobin was 31.3%, or about 30% of the original value, less than the average percentage decrease in number of red cells. This corresponds with an average increase in color index of 0.263 and an average increase in mean corpuscular volume of 22.9 cubic microns. The sedimentation rate of the blood cells increased markedly at the height of the anemia.

Bone marrow studies revealed striking alterations in the animals with severe anemia. The marrow of the long bones of the dog is normally fatty and fairly acellular. At the height of the experimental anemia the fatty marrow was completely replaced by solid, deep purple-red tissue, macroscopically indistinguishable from the marrow of cases of pernicious anemia. Histological studies showed proliferation of endothelial cells and of megaloblasts with little tendency to maturation. The histopathological picture was quite similar to that seen in cases of sprue anemia or in pernicious anemia.