Summary. (1) Mature rats produce more antihormone principle in response to injections of anterior pituitary-like gonadotropic preparations than rats which are immature when treatment is begun. (2) Of 2 gonadotropic preparations tested, the one containing a large amount of protein evoked less antihormone production but more precipitins than the one containing less antigenic material.

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Pathology of B_6 Deficiency in the Rat and Response to Treatment with 2-Methyl-3-Hydroxy 4, 5-Dihydroxymethyl-Pyridine (Vitamin B_6).

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Vitamin B_6 deficiency in rats was first described by György.[1] From the macroscopic appearance of the skin lesions he coined the term "rat acrodynia". Many investigators have since confirmed György's description of the symptoms. This investigation was initiated in order to study the histopathology of this deficiency and the histogenesis of the changes effected by synthetic vitamin B_6.

Twenty-one-day-old rats were placed on the following diet:

	%
Cornstarch	68
Purified casein	18
Crisco	8
Salt mixture	4
Cod liver oil	2

supplemented with 40 micrograms each of thiamin and riboflavin and 0.5 mg of nicotinic acid. No attempt was made to supply factor II in this series of experiments. The characteristic dermatitis became evident after 6 to 9 weeks. The animals were maintained on the deficient diet for 72 to 86 days. By this time the symptoms were very severe: The paws were denuded, edematous and moist, the ears thickened and scaly, the snout swollen and some ulcers present under the tongue. Many of the rats showed roughness and redness of the surface of the lower abdomen.

Histological findings: At this stage the epithelial cells of the *ears* were somewhat larger than normal. The stratum granulosum was wider and instead of the usual 1 to 2 layers in thickness, extended

[1] György, P., *Biochem. J.*, 1935, **29**, 741.

over 4 to 5 layers. Hyperkeratosis was extreme. The stratum lucidum was also thicker and on its external side faded imperceptibly into the stratum corneum. Intercellular edema was striking and acanthosis was present. In places there was necrosis, especially at the tips of the pinna. Polymorphonuclear leucocytic infiltration appeared, particularly in the necrotic regions. Frequently serum or polymorphonuclear aggregates were present in the region of the stratum granulosum, giving the appearance of serous and purulent vesicles. Edema with polymorphonuclear leucocytes was also present in the subcutaneous tissues. The hair follicles and sebaceous glands were inconspicuous.

There was a considerable increase in fat and histocytes about the cartilage. This area was edematous and hypervascularized. The perchondrial connective tissue layers were not distinct and appeared as edematous loose fibrous tissue. In places the cartilage was in contact with the hypervascularized adipose tissue. There were areas at which there was distortion and apparent loss of continuity of the cartilage.

Other animals from the same series showing the same severity of symptoms were fed with a single dose of 100 micrograms of synthetic vitamin B_6. Twelve hours later the number of mitotic figures increased. In 24 to 48 hours round cells were present in the subcutaneous tissue and the edematous state was barely discernible. In 3 days to one week, all of the ulcerations except the extensive ones were healed and the hyperkeratotic tissue peeled off in the form of plaques, leaving a smooth somewhat pinkish epithelial covering. The perichondrial tissue also showed rapid organization with disappearance of edema and inflammatory reaction. The hair matrix showed activity with hair regeneration and the atrophic appearance of the sebaceous glands was lost.

The skin changes of the paws and snout were essentially the same as those described on the ears. On the abdomen and back the skin showed atrophic changes both of the epidermis as well as of the hair follicles. The intercellular edema was also pronounced. After the administration of the synthetic B_6 the reaction of the skin in these areas was similar to that found in the ears. The tongue ulcerations showed a tendency toward slow healing.

These results indicate the healing of the skin lesions due to B_6 deficiency, following the administration of synthetic vitamin B_6. The animals have not been on the diet sufficiently long to develop lesions due to factor II deficiency. Since our results make it possible to single out lesions due to B_6 deficiency, they are of aid in differentiating the remaining members of the B complex from B_6.