

failed to protect the chicks against dermatitis and did not restore growth; when given to rats which had developed acrodynia on a vitamin B<sub>6</sub> deficient diet in daily doses of 1 mg or of 2 mg it failed to bring about a cure or restore growth. Following the publication of Elvehjem *et al.*, nicotinic acid has been tried in black-tongue and has been found to cure the mouth symptoms and restore appetite and weight. Although further tests must be made to determine whether the black-tongue preventive activity of liver extracts is due to nicotinic acid alone, the claim of Elvehjem *et al.*, that nicotinic acid cures black-tongue has been substantially confirmed. Thus direct test has shown that nicotinic acid prevents black-tongue but not chick dermatitis, proving that deficiencies of different factors underlie these two diseases, contrary to the conclusion of Koehn and Elvehjem.

As a result of this finding it now appears that under the heading of vitamin B<sub>2</sub> as defined after its separation from vitamin B<sub>1</sub> four factors are grouped if the human pellagra-preventive factor should be identical with the black-tongue preventive factor, or five factors if these two should prove to be distinct. Evidence of their identity is circumstantial, of the type which in the past led to belief in the identity of other pairs of these factors until further chemical purification led to a separation. Only the cure of both diseases by one and the same crystalline material can prove finally that they are caused by deficiency of a common factor.

Assuming that the black-tongue preventive and pellagra preventive factors are identical, it appears that vitamin B<sub>2</sub> comprises four entities. Two of these, flavin and nicotinic acid, have been isolated and identified. Two more have been distinguished but not isolated: these are the vitamin B<sub>6</sub> (preventive of rat dermatitis) and the factor preventive of chick dermatitis. Neither of these is identical with flavin, as shown by the work of György<sup>4</sup> and of Koehn and Elvehjem,<sup>5</sup> respectively. Our observations now show that neither is identical with nicotinic acid. If clinical tests show that nicotinic acid is pellagra-preventive, the list will be complete; but if it is not, the pellagra preventive factor must be added, making a total of five.

On account of its supposed identity with the pellagra-preventive factor, Elvehjem and Koehn have used the name vitamin B<sub>2</sub> to denote the chick pellagra-preventive factor. Since we have shown these factors to be distinct, there remains no single reason to support this usage, and in view of early definitions the name vitamin B<sub>2</sub> should be used to denote the complex made up of all the factors mentioned above. If it is used for any single factor, then it should be reserved for the human pellagra preventive factor.

A detailed report of our observations will be published elsewhere.

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### SPONTANEOUS LEPROSY IN A MOUSE

A SPONTANEOUS leprosy-like disease in rats is very well known. It was first described by Stefansky<sup>1</sup> in 1903 at Odessa and almost simultaneously and independently by Dean<sup>2</sup> in England. Subsequent reports by various authors have established its wide-spread distribution in different parts of the world.

Two varieties of the spontaneous disease have been described, the musculocutaneous and glandular. In the former, there is extensive involvement of the skin, subcutaneous tissues and skeletal muscles with associated alopecia, ulceration and loss of subcutaneous fat. In the other form there is extensive lymphatic glandular involvement, both focal and more universal, but chiefly confined to those of the axilla, groin, neck and submaxillary regions. This division is, however, not very strict. The lymphatic glands are involved in the cutaneous form and the skin to a mild degree in the glandular type. In both there is visceral involvement as well.

A similar disease in the closely related mouse has hitherto not been described.

A brown wild house mouse (*mus musculus*) was found wandering through our laboratory in broad daylight. It was evidently deformed, sickly in appearance and could readily be caught. It presented all the features of the musculocutaneous variety of the disease, as seen in the rat. There were alopecia and thickening of the skin of the scalp with distortion of the pinnae and patchy areas of alopecia over the skin of the back with two discrete gray circular ulcers, measuring on the average 0.15 cm in diameter. The anterior pubic and perineal regions were enormously thickened and prominent. The base of the tail was in consequence deviated to the right. Both hind limbs, particularly in the femoral and tibial regions, were likewise greatly thickened and nodular. The forelimbs were involved, but to a lesser degree. Sections through the skin revealed diffuse infiltration of the subcutis by softish yellowish-white tissue. In the scalp both corium and subcutis down to calvarium were thus infiltrated and thickened. In the forelimbs the corium was less involved; the subcutis, however, was quite markedly thickened and infiltrated. In the hind limbs, there was minimal involvement of the corium which could readily be stripped from the underlying, greatly infiltrated, tissues. The cutis, subcutis and all struc-

<sup>3</sup> *Jour. Biol. Chem.*, 114: 109, 1936.

<sup>4</sup> *Biochem. Jour.*, 29: 745, 1935.

<sup>5</sup> *Jour. Biol. Chem.*, 108: 709, 1935.

<sup>1</sup> W. K. Stefansky, *Centralblatt f. Bakt. und Parasitenkunde*, 33: 481, 1903.

<sup>2</sup> G. Dean, *Centralblatt f. Bakt. und Parasitenkunde*, 34: 222, 1903.

tures down to the pelvic and sacrococcygeal bones were replaced by a similar alveolated whitish tissue, which surrounded and narrowed the anogenital canals. The pelvis and its contents, however, were uninvolved. The inguinal (left), lumbar and iliac lymph nodes were considerably enlarged. Both uterine horns were thickened and nodular. There was otherwise no other gross visceral involvement. X-rays confirmed the soft tissue thickenings in the regions cited above, but failed to demonstrate lesions of the bones or joints.

In sections of skin examined microscopically there is massive infiltration of corium and subcutis by large pale monocytic cells similar to the lepra cells described in the rat. These possess a stippled, somewhat basophilic cytoplasm stuffed with acid-fast bacilli when stained by Ziel-Neelsen. The bacilli are delicate rods, occasionally curved, measuring 1.5–5.4  $\mu$  in length. They are more or less concentrically and closely packed within the cell. The cigar-like bundles of bacilli and globi of the human lepra cells are not seen.

Within these areas of extensive cellular infiltration, there are practically acellular zones made up of masses of acid-fast bacilli. Commonly within and about these areas there are lepra cells with karyorrhexis of the nucleus. In the well-preserved cells the nucleus is eccentric, oval or spherical, occasionally compressed and deformed. Only strands of atrophied collagen course through the infiltrative areas, except in instances where the immediate subepidermal zones of the corium are relatively spared. The epidermis is markedly atrophied and the papillae are obliterated in sections of skin where the infiltration extends to the epidermis. The cutaneous appendages in such instances are often lost or atrophic. The perineural sheaths of otherwise intact nerve fibers are infiltrated by lepra cells. There is moderate involvement of the skeletal muscle. Perimysium and endomysium, particularly adjoining the subcutis, are heavily infiltrated by lepra cells leading in instances of greater infiltration to atrophy and loss of muscular fibers. Portions of an axillary and sections of lumbar and iliac lymph nodes are diffusely and heavily infiltrated by lepra cells. Practically all other organs are involved to a degree. There are single and groups of lepra cells in the myocardium, lung (peribronchial, perivascular and interstitial), spleen, pancreas, liver (conglomerate groups more frequently adjoin larger venous radicles, chiefly hepatic, and numerous Kupffer cells are stuffed with bacilli), kidney (chiefly in glomeruli), adrenal, ovary, uterus (largely in the thickened endometrium), serosa of peritoneum, paravertebral muscles (largely at musculo-periosteal junctions), paraganglia and bone marrow (as scattered single cells). The dorsal ganglia and spinal cord are not involved, except for the perineural sheaths of spinal nerves. Intravascular poly-

morphonuclears and monocytes infrequently contain acid-fast bacilli.

Mice were inoculated with an emulsion of the lesions, and at present the course of the experimentally-induced disease is being studied in mice and rats. It is known that the rat strain of leprosy can be induced in all other types of rats. The mouse is, however, essentially refractory. It will be of interest to determine whether this is as specific a strain for mice as the murine form is for rats.

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### ENCEPHALIZATION OF BRIGHTNESS DISCRIMINATION IN MAMMALS

It is well known in comparative neurology that in mammals the visual system, like other systems, shows an orderly and progressive development in structure. Although the point to point projection of the retina on the lateral geniculate body, the striate area and the superior colliculus, is as exact in lower as in higher forms,<sup>1,2,3</sup> there do appear certain systematic differences in structural organization. These differences appear to be quantitative rather than qualitative. For example, passing up the phylogenetic scale it is found that the proportion of uncrossed fibers of retinal origin increases. We have, then, an increase in the size of the binocular projection fields in the primary visual centers. There is also an increase in the size of the geniculo-striate complex at the expense of the lower visual centers and a gradual merging of the pretectal area with the superior colliculus.<sup>4</sup>

On the basis of this structural development of the visual system as we pass up the phylogenetic scale, it might well be expected that there would be a parallel change in the functional importance of the various visual stations. The doctrine of encephalization would lead one to suspect that in the lower mammals the subcortical visual centers would be of relatively greater importance, and passing up to the primates the geniculo-striate complex would gradually become dominant. The facts, however, do not support such a view, at least in the discrimination of differences in the intensity of lights. The evidence indicates that even in the rat the geniculo-striate complex alone mediates the brightness discrimination habit in the intact animal. This is shown by the following facts. After the brightness discrimination habit has been formed, de-

<sup>1</sup> K. S. Lashley, *Jour. Comp. Neur.*, 59: 341, 1934.

<sup>2</sup> K. S. Lashley, *Jour. Comp. Neur.*, 60: 57, 1934.

<sup>3</sup> B. Brouwer, "Anatomical, Physiological and Clinical Studies on the Central Nervous System." Baltimore: 1927.

<sup>4</sup> C. U. Ariëns Kappers, G. C. Huber and E. C. Crosby, "The Comparative Anatomy of the Nervous System of Vertebrates." New York: 1936.