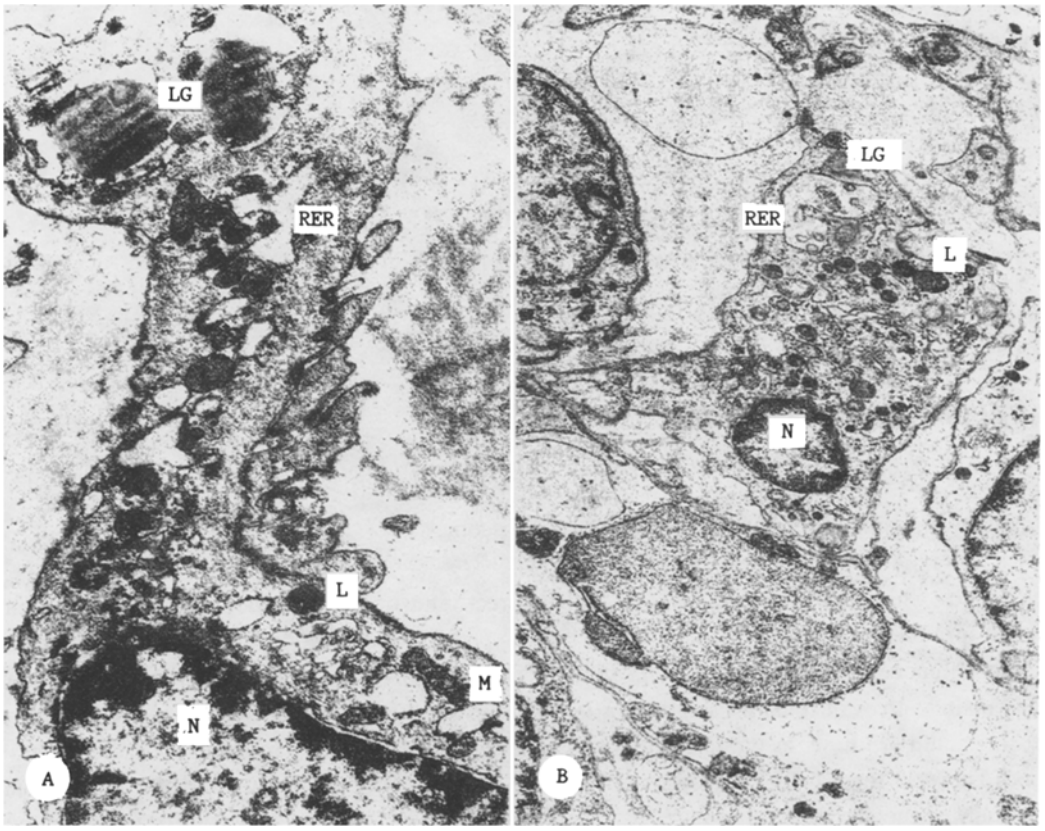

Fig. 1. Ultrastructure of interstitial cells of the renal medulla. A) Intac animals. 30,000×. B) 30 min after injection of Lasix. 20,000×; N) nucleus, M) mitochondria, L) lysosomes, LG) lipid granules, RER) rough endoplasmic reticulum.

The most specific subcellular structures of the interstitial cells are lipid granules and lysosomes. The relative proportions of these structures may serve as a criterion of the prostaglandin-synthesizing activity of the interstitial cells, i.e., an increase in the number of lysosomes together with a decrease in the number of lipid granules in the interstitial cells are evidence of activation of prostaglandin synthesis [3].

An electron-microscopic investigation of the interstitial cells 30 min after a single injection of Lasix revealed a marked increase in the number of lysosomes against the background of a sharp decrease in the number of lipid granules. Developed components of the endoplasmic reticulum and Golgi complex were seen in this case in the cytoplasm of the cells (Fig. 1b). Thus, after a single injection of Lasix, predominance of lysosomes over lipid granules could be seen in the interstitial cells against the background of developed organelles. Activation of prostaglandin production in response to a single injection of Lasix has been demonstrated also by other workers [6].

By contrast with a single injection, during long-term (30 days) injection of Lasix, two types of interstitial cells were found in the internal renal medulla. The first type was closely similar in ultrastructure to the interstitial cells described in the experimental animals of group 2. However, fewer lysosomes and lipid granules were seen in their cytoplasm than in the animals of group 2, although quantitatively speaking, lysosomes predominated in this case over lipid granules. Changes of this kind are evidence that during long-term administration of Lasix, prostaglandin production by the interstitial cells was weaker than after a single injection.

A distinguishing feature of the type 2 cells is the presence of a developed rough endoplasmic reticulum, occupying its basal part, in their cytoplasm. Lipid granules typical of interstitial cells were found in single numbers or were completely absent (Fig. 2). Close to the cells there were coarse bundles of collagen fibers, lying in the thickness of the amorphous intercellular substance (Fig. 3a, b). Meanwhile, besides the types of interstitial cells described above, no other cells could be identified in the interstitial tissue, whose structure might suggest the synthesis of intercellular components of connective tissue and, in particular, collagen fibers. On the basis of analysis of these results, we consider that some of the interstitial cells, during long-term activa-

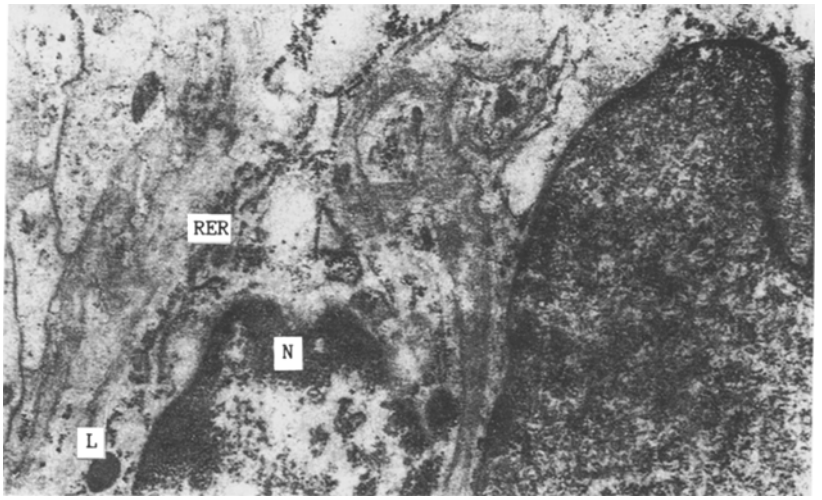

Fig. 2. Ultrastructure of type 2 interstitial cells of the renal medulla during long-term administration of Lasix. 30,000×.

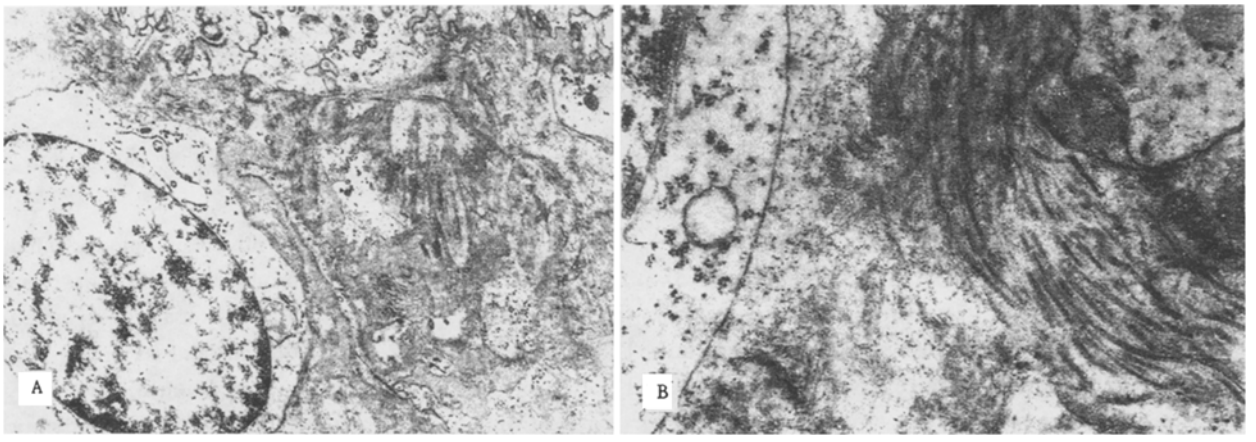

Fig. 3. Enlargement of noncellular components of connective tissue in interstitial tissue of inner zone of renal medulla during long-term injections of Lasix. A) Collagen fibers and amorphous intercellular substance. 20,000×; B) Coarse bundles of collagen fibers. 30,000×.

tion by diuretics, may switch to the production of intercellular connective-tissue components. This may evidently be one of the causes of the development of sclerosis in the renal papilla.

Thus, a single injection of Lasix stimulates prostaglandin synthesis by the interstitial cells. Long-term stimulation ultimately leads to a relative decrease of prostaglandin production in the interstitial cells, by comparison with a single injection of Lasix. Under these circumstances a second population of these cells if formed, oriented toward the production of connective-tissue proteins and glycosaminoglycans. It was suggested previously that interstitial cells, being elements of mesenchymal origin, specialized for prostaglandin synthesis, preserve their ability to produce components of the interstitial substance of the medulla [5].

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ANTICONVULSANT EFFECTS OF NEUROTROPIN

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KEY WORDS: neurotropin, epileptic activity, picrotoxin, bicuculline, strychnine, metrazol, kainic acid

The possibility of suppressing epileptic activity by substances of endogenous origin has now been demonstrated [1, 2, 5, 6]. One preparation, obtained from rabbit skin inoculated with cowpox virus, is neurotropin, produced by the firm "Nippon Zoki Pharmaceutical Limited" [7]. Neurotropin possesses a broad spectrum of biological activity. Besides its antiallergic and anti-inflammatory action, neurotropin also affects brain function. The antistressor action of neurotropin and its beneficial effect in experimental cerebral edema in mice have been established [11]. Neurotropin acts selectively on brain electrical activity [6].

The aim of this investigation was to study the effects of neurotropin on generalized and local forms of epileptic activity induced in animals of different species (rats, mice, cats).

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats (270-320 g), C5BF6 mice (18-22 g), and cats (2.5-3.2 kg) under acute conditions. Seizures were induced by intraperitoneal injection of picrotoxin ("Serva," West Germany) 4.0 mg/kg, bicuculline ("Serva") 4.0 mg/kg, metrazol 60 mg/kg, or kainic acid ("Sigma," USA) 15 mg/kg. Seizures were recorded visually for 1 h after the injection of the convulsants. The latent period of the first seizures, their maximal intensity, and the number of animals developing seizures were determined. The intensity of the seizures was estimated by the use of a five-point scale [4]. Foci of epileptic activity were induced by application of a piece of filter paper (2 × 2 mm), soaked in 0.1% strychnine nitrate, to the cerebral

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