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Morphogenesis and ultrastructure of the peripolar cells in the mouse kidney

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Summary. Peripolar cells are located in the outer layer of the Bowman's capsule. They surround the vascular pole of the renal corpuscle and project into the urinary space. Morphologically they are characterized by the presence of secretory granules within their cytoplasm. In order to study their embryological development, we used 60 C57bl mice embryos (15th to 19th gestational day), 10 newborn mice (2 hours to 6 days old), 10 preadult mice (8-30 days old) and 4 adults (4 months old). Some granular cells, dispersed at the outer and inner layer of the Bowman's capsule, appear on the 17th gestational day. Later, these cells are found around the vascular pole of the renal corpuscle, located exclusively at the outer layer of the Bowman's capsule. Their granules are spherical and variously dense, they are surrounded by a membrane and their number increases progressively with time and reaches a maximum on the 4th postnatal day. Following that, there is a diminution and then their population stabilizes. By the end of the first month, there are only a few such cells (mean number 1 to 2). They become smaller and they always project into the urinary space.

Key words: Peripolar cells, Embryology, Renal corpuscle

Introduction

The peripolar cells, which have been described recently, are found in the parietal Bowman's capsular epithelium, forming a cuff around the vascular pole of the glomerulus. Their prominent morphological characteristics are cytoplasmic granules, the composition of which has not been discovered yet, but it is suggested that these cells may release factors which modulate secretory or absorptive functions of the renal tubules (Ryan et al., 1979, 1982).

The peripolar cells have been observed in quite a few mammals (Ryan et al., 1982) and amphibia (Hanner and Ryan, 1980). Their embryological development has been observed only in sheep, because in the fetal lamb the peripolar cells are detectable at an early stage of gestation (Mitchell et al., 1982).

Because of their site, the peripolar cells are brought into close relation to the juxtaglomerular apparatus. In the present work, we have studied the ultrastructure of the peripolar cells in mice during their embryological development, as well as the possibility of their having a relationship with the cells of the juxtaglomerular apparatus. Some comparative observations concerning the development of the juxtaglomerular apparatus and the peripolar cells, were also made.

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Materials and methods

Sixty mice embryos and twenty adult mice were used. The age of the embryos ranged from 15 to 19 days and the age of the newborn mice ranged from 2 hours to 30 days. The mice were anaesthetized with ether and fetuses were delivered by Caesarian section. The kidneys were removed while the fetuses or the mice were anaesthetized.

The kidney tissue-pieces were immersed in fixative immediately after their removal. The fixative consisted of 3% glutaraldehyde in sodium phosphate buffer at pH 7.3. Each embryonal kidney and piece of kidney was further cut into smaller pieces (1 mm in width), taking care to include the whole width of the cortex in each piece. The tissue pieces were fixed for 2 hours at 4° C, washed for 20 minutes in sodium phosphate buffer, postfixed for 1.5 hours in 2% phosphate-buffered osmium tetroxide and then stained with 1% aqueous uranyl acetate for 14-18 hours (in tissue staining). They were consequently dehydrated in a series of aqueous alcohol solutions and finally with 100% alcohol, and then embedded in Epon 812 (Serve, Feinbiochemica,

Heidelberg). Semithin sections (1-1.5 μm) were stained with aqueous solution of 1% toluidine blue and 1% borax. Thin sections (80 nm) were cut in an LKB ultramicrotome, they were stained with lead citrate (Reynolds) and examined in a Jeol 100CX TEM, at 80 kv.

Results

The mouse renal corpuscles of metanephros began to differentiate on the 15th gestational day. During the III phase of their development, in the cytoplasm of some cells of the inner and outer layer of the Bowman's capsule, granules appeared, while their overall appearance was otherwise relatively undifferentiated (Fig. 1). Initially, they were found in the outer and inner layer of the Bowman's capsule, until the 19th gestational day (Fig. 2), when they were located only in the outer layer of Bowman's capsule. Postnatally, these cells were solely located at the vascular pole of the renal corpuscle and they protruded into the urinary space (Figs. 3, 4).

These granular cells, in the initial stages of differentiation, were large and connected to the still undifferentiated neighbouring cells of the outer Bowman's capsule by desmosomes (Fig. 1). They contained a large nucleus with abundant euchromatin and their cytoplasm contained a great number of polyribosomes, rough endoplasmic reticulum, Golgi apparatus with transportative and secretory vesicles, mitochondria, lysosomes, microtubules and microfibrils, mainly at the periphery of the cell. As the differentiation progressed, the cells became smaller and protruded into the urinary space. Their overall number increased immediately after birth, and then was reduced to 1 to 2 cells which were located at the vascular pole of the renal corpuscle (Figs. 2, 5, 6). After the 2nd postnatal day there was an increase in the number of the microfibrils, which formed bundles, located mainly at the cell periphery, in the vicinity of the basement membrane. The granules were spherical or ovoid and surrounded by a membrane (Figs. 2, 6, 7). Their number was initially reduced but gradually, during the gestational life, increased. Immediately postnatally they increased, reaching a peak on the 2nd to 4th day (Fig. 4). Following that, there was a small diminution of their number finally reaching the adult quantity. The granules initially presented a variation in their density, ranging from dark to light. Gradually, as the differentiation progressed, they became denser.

Discussion

The peripolar cells, as well as the rest of the cells of the outer layer of Bowman's capsule, result from the differentiation of the mesenchymal cells which are located in the vicinity of the developing vascular pole of the renal corpuscle, at the outer loop of the S-shaped body. The study started on the 15th gestational day. This period of development corresponds to the approximate beginning of the metanephric differentiation in the mouse (Zamboni and Upadhyay, 1981).

Secretory cells containing granules and located at the outer as well as at the inner Bowman's capsule, were initially traced on the 17th gestational day. As the differentiation progressed, the cells were exclusively located at the outer layer of the Bowman's capsule and around the vascular pole whence their name peripolar. This name was introduced by Ryan et al. (1979), who were the first to describe and study these cells in rats. Later they have been described in other species (Gall et al., 1986; Morild et al., 1988; Christensen et al., 1989). Granular cells, dispersed at the outer and inner layer of Bowman's capsule in developing renal corpuscles of rats, were also observed by Dhiab al Naimy and Bearn (1980, 1981) who describe them as «glomerular granular cells» and which disappeared before birth. This is in accordance with our results, since the granular cells were initially dispersed, but soon collected at the vascular pole, which is the typical position of the peripolar cells.

The peripolar cells in the mouse appear immediately after the appearance of the juxtaglomerular cells, which happens on the 16th gestational day (Minuth et al., 1981; Sioga, 1985). On the contrary, in the sheep, which is an animal presenting a longer gestational period and poor development of the juxtaglomerular cells, the peripolar cells appear on the 53rd gestational day (duration of gestation 147 days), very much earlier than the time of appearance of the juxtaglomerular cells, which become evident on the 92nd gestational day (Mitchell et al., 1982). This difference is probably due to the different final population of these cellular groups.

The peripolar cells, from the beginning of their differentiation, are in close morphological relation to the juxtaglomerular granular cells, from which they are sometimes separated only by their basement membrane. This topography resulted in suggesting that there could be a functional interrelation. Immunohistochemical studies proved that in the sheep (Gall et al., 1984) as well as in man (Gardiner and Lindop, 1985) the granules of the peripolar cells do not contain renin. Recent immunohistochemical studies show that these cells probably contain kallikrein or a similar polypeptide (Gall et al., 1984). Kallikrein is also traced in the cells of the distal convoluted tubules, but its functional role is not elucidated. Okamura and Inagami (1984) suggest that renal kallikrein causes the selective release of active renin, which explains the close morphological relation between the juxtaglomerular granular and the peripolar cells. Nevertheless it does not explain the earlier differentiation of the juxtaglomerular cells in the mouse.

Briggs et al. (1984) support the view that kallikrein deactivates the natriuretic peptides and participates in the regulation of Na^+ (natriuretic activity). This view is supported by Hanner and Ryan (1980) and Hill et

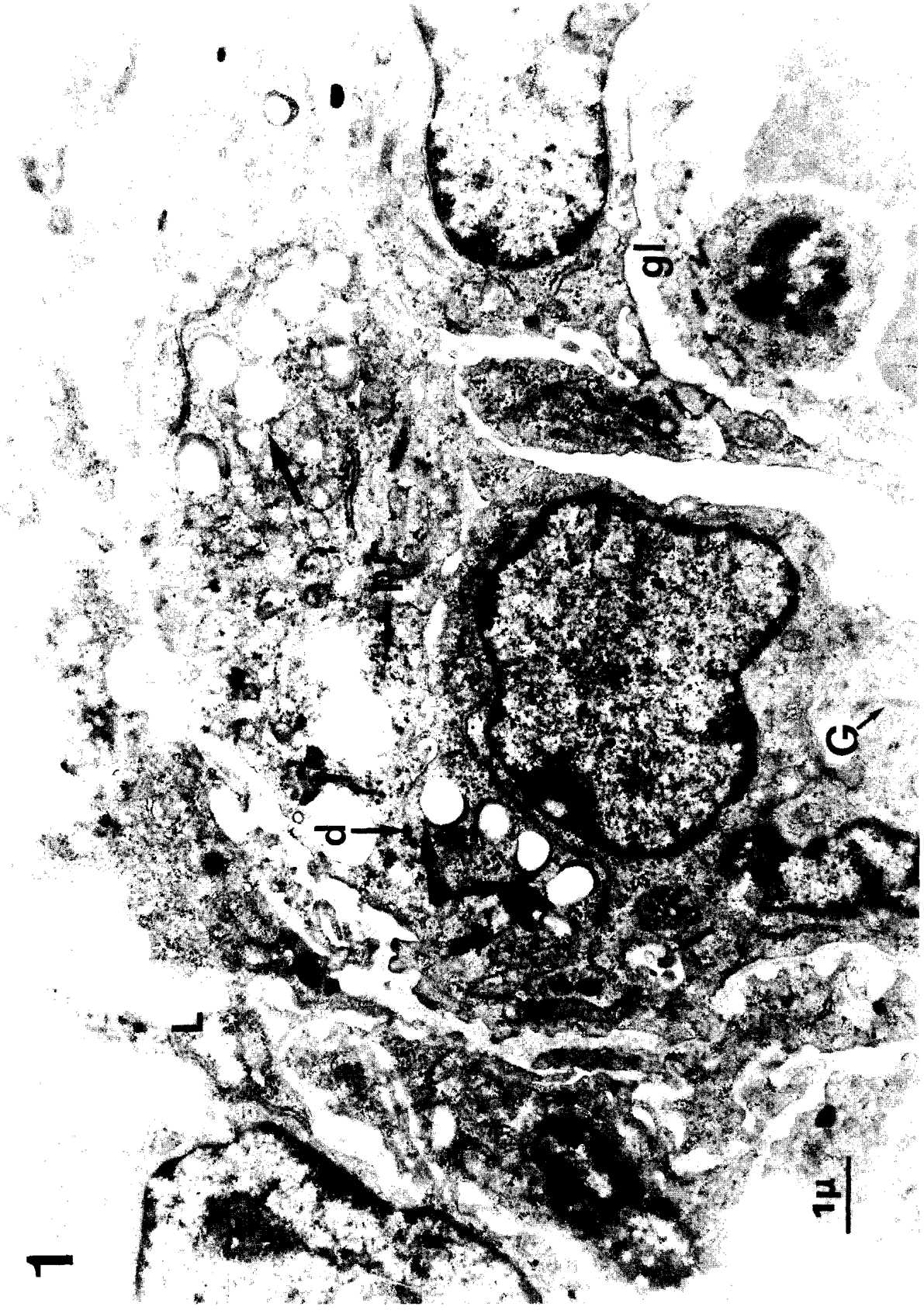

Fig. 1. Juxtaglomerular region on 18th gestational day. Parietal epithelium of Bowman's capsule with granules (arrows). Lacis cells (L), polyribosomes (pr), Golgi complex (G), desmosomes (d) between peripolar cells, glomerulus (gl). × 12,000

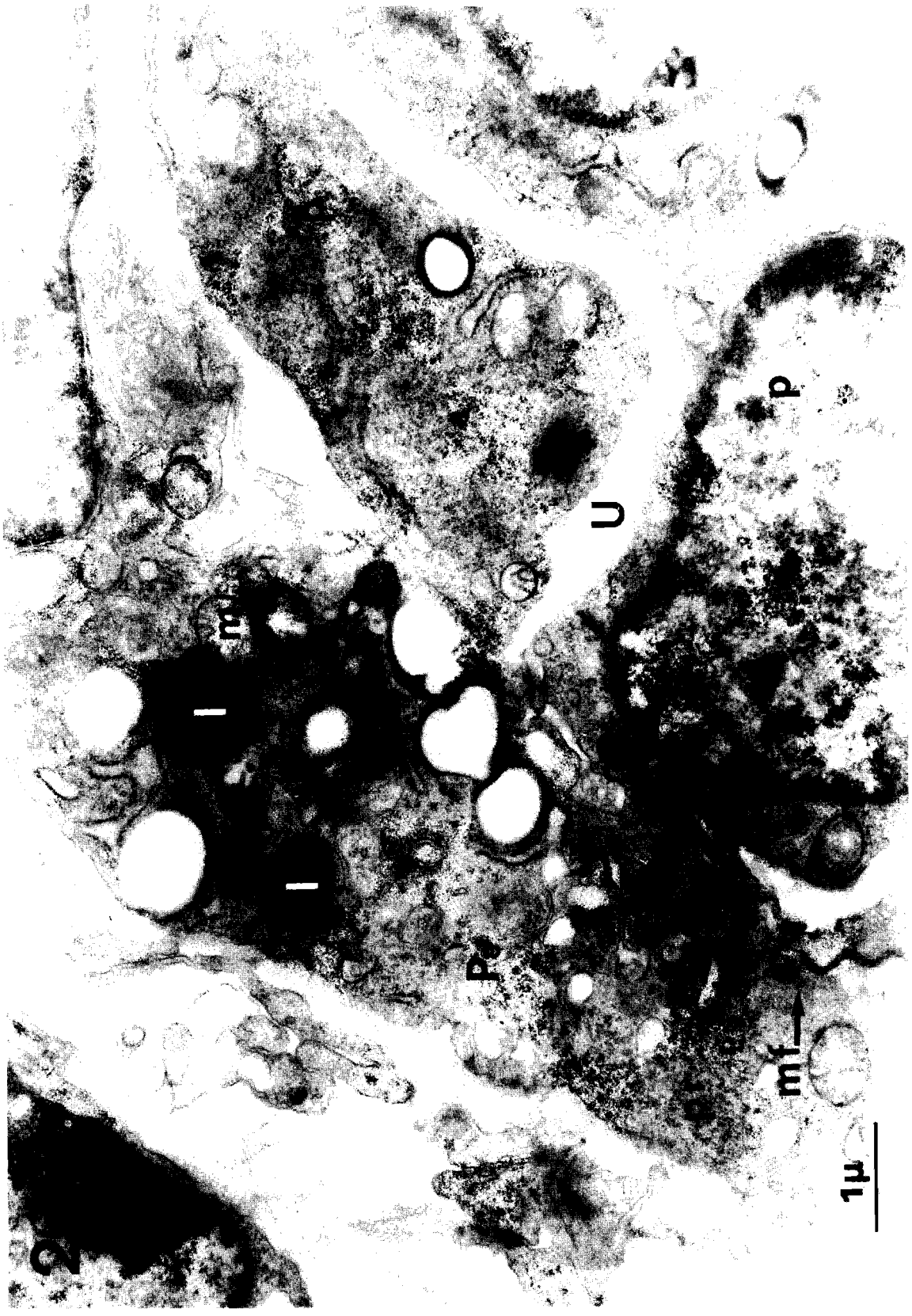

Fig. 2.
A developing renal corpuscle in the 19th gestational day. Parietal epithelium (Pe) with granules, urinary space (U), lysosomes (l), polyribosomes (pr), microfilaments (mf), mitochondria (m), podocytes (p). × 18,000

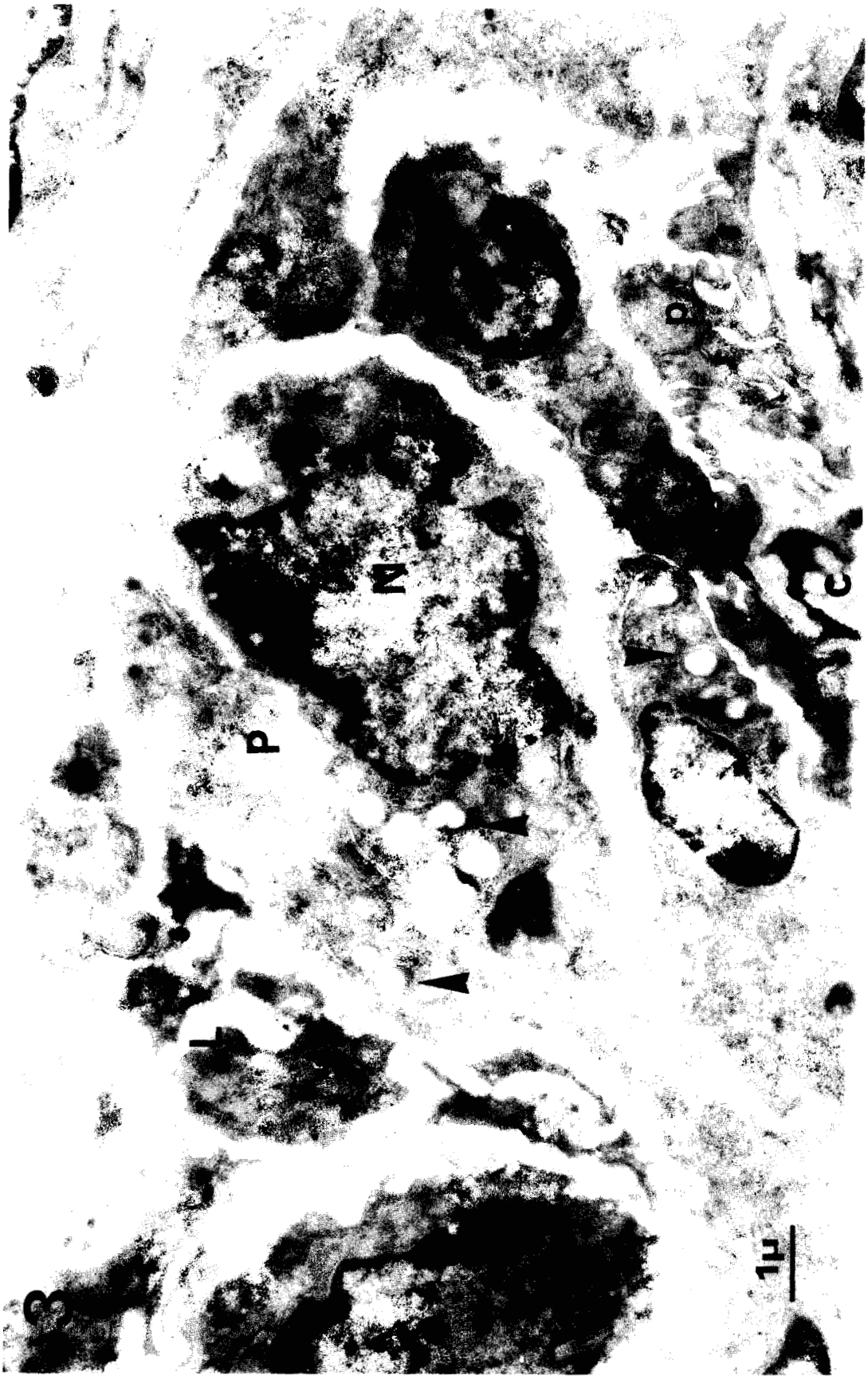

Fig. 3. Vascular pole of a developing renal corpuscle from a 2-day-old mouse. Peripolar cells (P) with granules (arrows), lacis cells (L), capillary (c), podocytes (p), nucleus (N). × 12,000

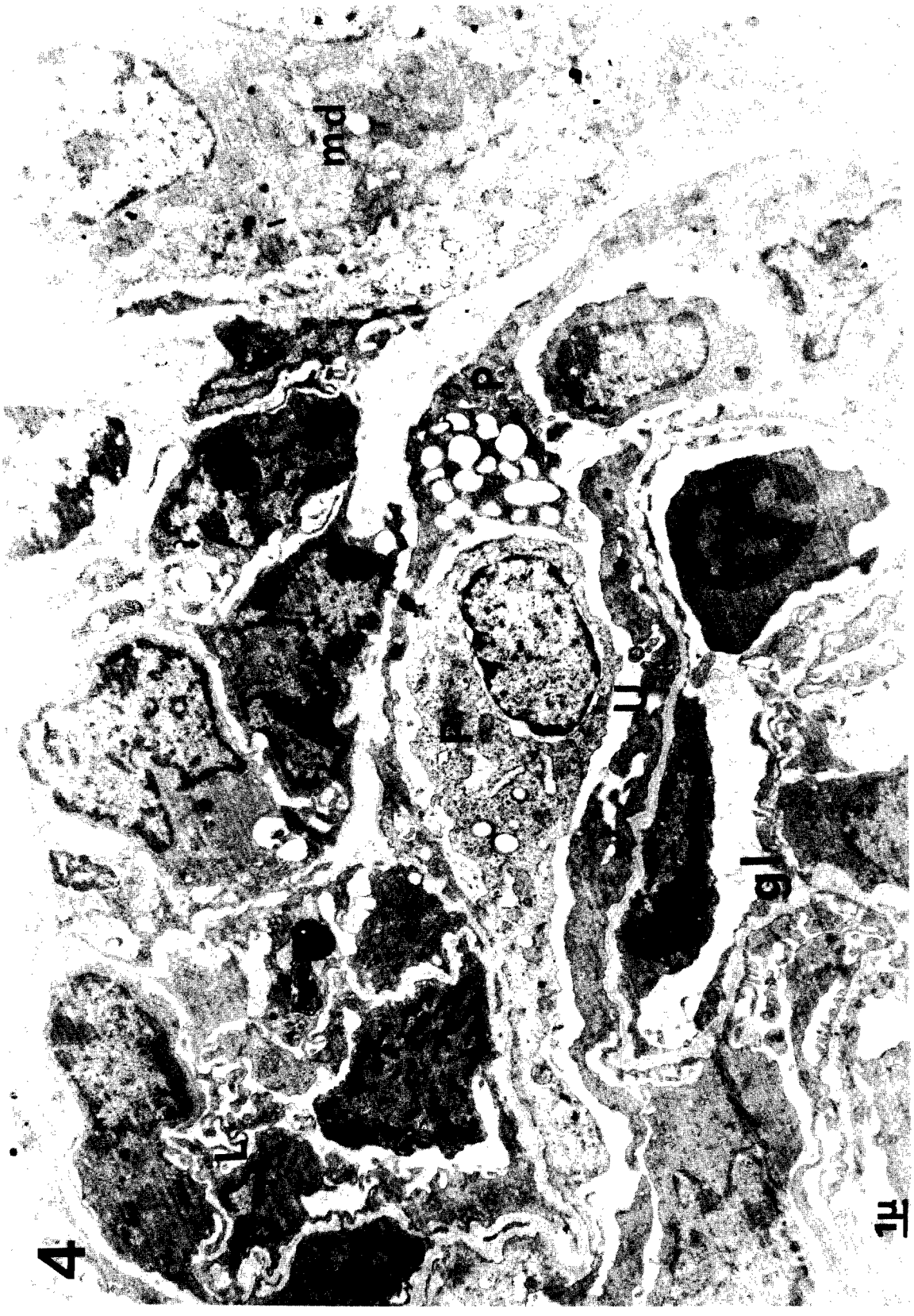

Fig. 4. Vascular pole of a developing renal corpuscle from a 4-day-old mouse. Peripolar cells (P), lacis cells (L), urinary space (U), glomerulus (gl), macula densa (md). × 6,000

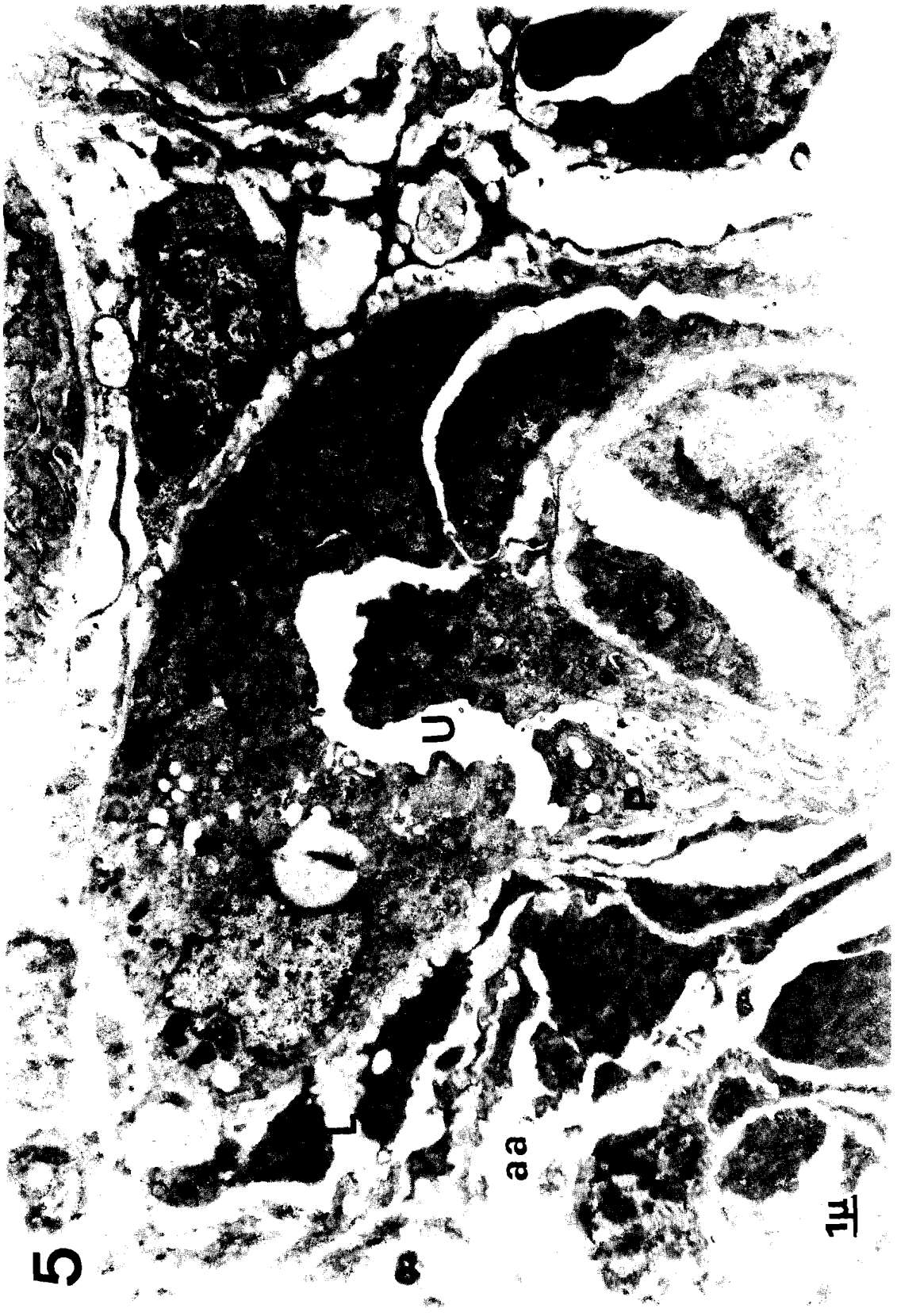

Fig. 5.
Peripolar cells (P) in the vascular pole of a renal corpuscle from an 8-day-old mouse. Lacis cells (L), urinary space (U), afferent arteriole (aa). × 6,000

Fig. 6. Peripolar cells (P) in the vascular pole of a mature renal corpuscle from a one-month-old mouse. Urinary space (U), macula densa (md), glomerulus (gl). × 30,000

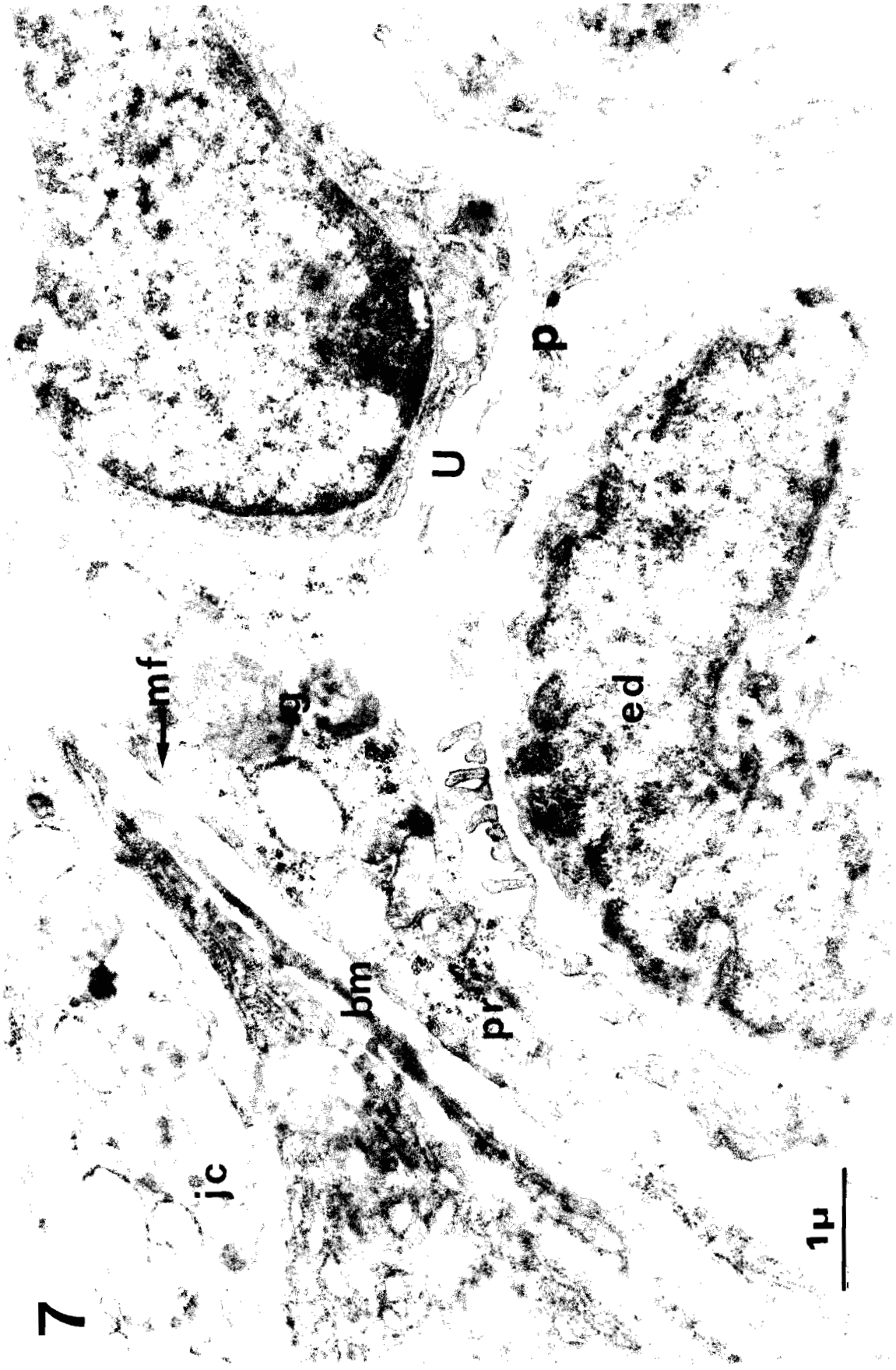

Fig. 7. Peripolar cells in a 6-day-old mouse. Basement membrane (bm), polyribosomes (pr), granules (g), microfilaments (mf), podocytes (p), urinary space (U), endothelium (ed), juxtaglomerular granular cells (jc). × 20,000

al. (1983) who found that there is hypersecretion of the peripolar cells in animals receiving food without Na^+.

Rapid development and distinct growth of the peripolar cells was observed by Alcorn et al. (1984) in newborn sheep. This was also a finding in this study, since the number of the peripolar cells as well as the number of their granules increased rapidly after birth. This is probably due to the augmented needs for H_2O and electrolytes immediately after birth, in comparison with the needs during gestation, when the embryonic kidney can fully compensate by producing the proper quantity of N_a^+, water and acid, which are needed for preserving the water and electrolytic balance (Kleinman, 1978; Spitzer, 1982). The low arterial pressure, along with the low rate of Na^+ release from the cells of the distal convoluted tubules, are also factors exciting the renin-angiontensin system. These functional aspects are confirmed by the morphological evidence, which showed that the juxtaglomerular granular cells have a linear increase up to the maturation time (Bruhl et al., 1974; Sioga, 1985; Dhiab al Naimy and Bearn, 1986).

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