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Endothelial Inclusions in Congenital Infantile Nephrosis

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Summary. Electron microscopic studies on renal tissue, obtained by percutaneous biopsy from a patient with *Congenital Infantile Nephrosis*, have revealed the presence of round and/or tubular bodies in the cytoplasm of endothelial cells of the glomeruli.

The bodies generally occur as aggregates in an apparent association with the endoplasmic reticulum. Also, other profiles were observed. It is believed that they represent one of the many images of a system of undulating tubules.

Sinces these bodies occur irrespective of the presence of virus particles in the tissue under study, it is concluded that they are not viral in nature.

An electron microscopic study on renal tissue, obtained by percutaneous biopsy according to the method advocated by Kark and Muehrcke (1954), from a patient with *Congenital Infantile Nephrosis*, has revealed the presence of membrane-bound cytoplasmic inclusions in the endothelial cells of the glomerular capillaries.

An area from two glomerular capillaries is shown in Fig. 1. The endothelium of the upper capillary contains aggregates of small round bodies, some of which appear to be "hollow." These aggregates are delimited by a single, smooth membrane which at some points is continuous with elements of rough surfaced endoplasmic reticulum. These round bodies frequently produce crystalline arrays. At higher magnifications, some of these structures appear to be round, smooth membrane bound structures with electron-lucent cores (Inset, Fig. 1). Profiles of other bodies, however, indicate that they may not be spherical but rather tubular. A comparison of the two micrographs profoundly suggests that the crystalline array of granules is the result of a transverse plane of section passing through a system of tubules. Both the tubules and the granules measured approximately 25 mμ in diameter. The undulating nature of the tubules was most clearly depicted in longitudinal sections (Inset, Fig. 1). Elements of endoplasmic reticulum appeared to be "continuous" with the array of tubular structures. Occasionally, the plane of section was such as to produce images of greater complexity. In addition, circular profiles bound by two membranes were present. A careful examination suggested that those profiles were formed by two undulating tubules lying within the thickness of the section, such that the crest of one lies opposite the trough of the other.

Observations of crystalline, reticular or tubular arrays within the endoplasmic reticulum of endothelial and other cells, similar to the ones observed in the biopsy material at hand, or of somewhat modified structure have been made in a variety of conditions.

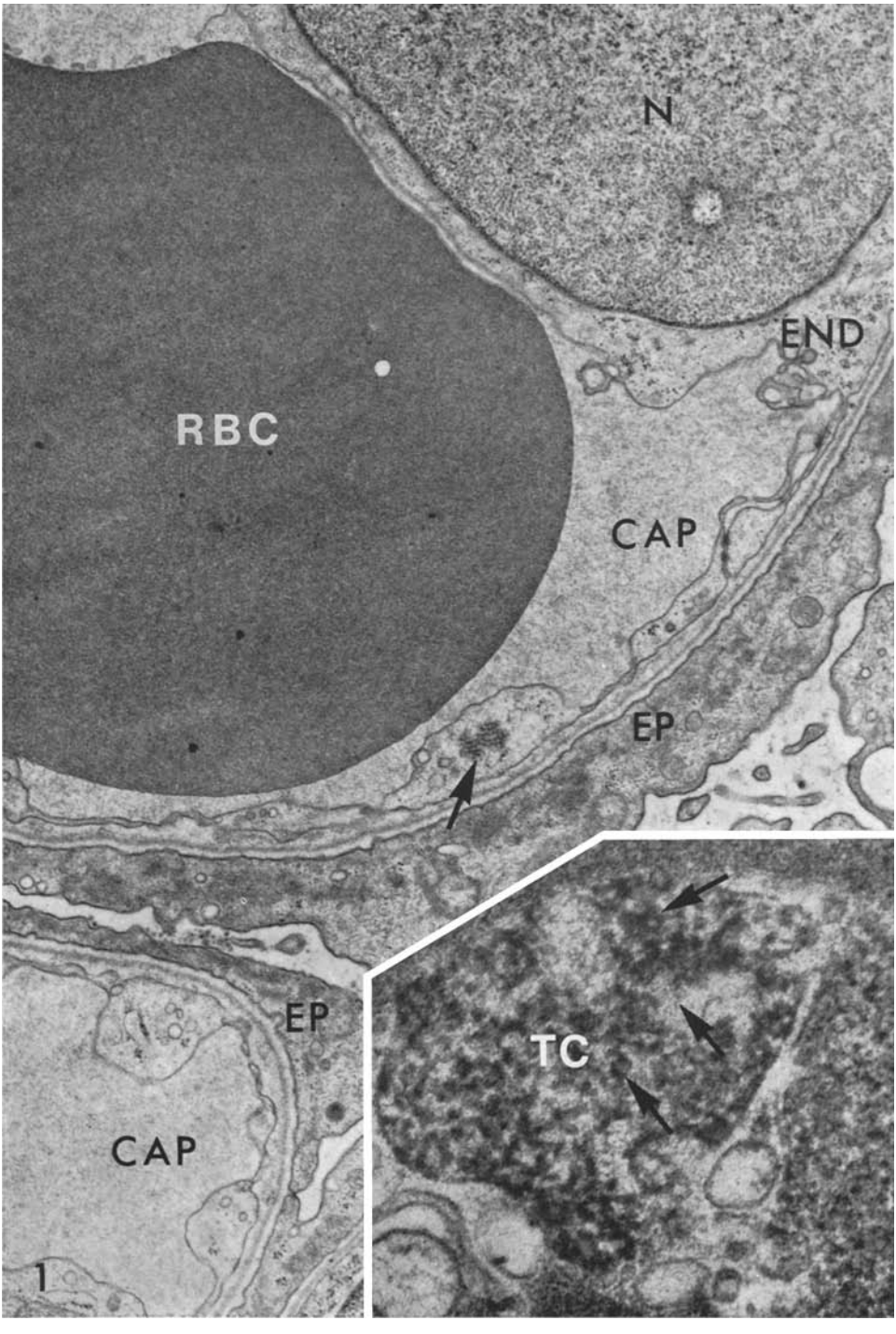

Fig. 1

Among the circumstances in which such structures are encountered are normal human cells (Chandra, 1968), normal monkey tissue (Ishikawa, 1963; Sebuwufu, 1968; Finegold, 1967; de Martino *et al.*, 1969; Rosen and Tisher, 1968; Battifora and Markowitz, 1969); kidney tissue in SLE (deMartino *et al.*, 1969; Hurd *et al.*, 1969; Norton, 1969; Sinkovics *et al.*, 1969; Pincus *et al.*, 1970; Györkey *et al.*, 1969; Grausz *et al.*, 1970; Kawano *et al.*, 1969; Haas and Yunis, 1970; Datsis, 1972a); lipoid nephrosis (deMartino *et al.*, 1969; Duffy, 1969); syphilitic nephrosis (Datsis, 1972b); Chronic Glomerulonephritis (Datsis, 1972c); and other renal diseases (Battifora and Markowitz, 1969; Hurd *et al.*, 1969; Shearn and Stephens, 1970; Norton, 1969); sarcomas (Chandra, 1968; Moore and Chandra, 1968; Munroe *et al.*, 1964; Lombard *et al.*, 1967; Bucciarelli *et al.*, 1967); lymphomas (Chandra, 1968; Kakuk *et al.*, 1968); leukemias (Recher *et al.*, 1968; Uzman *et al.*, 1968; Siegal *et al.*, 1968); a variety of viral infections, and in experimental nephrotoxicity studies (Datsis, 1972d).

The morphologic character of the aggregates has presented a wide spectrum of variations in the different circumstances in which they have been found. In normal tissues, neoplastic conditions and in virus-infected tissues they have usually been described as a rather tightly packed array of particles that have only rarely been recognized as tubular in nature (Chandra, 1968). In contrast, in most of the material from patients with Lupus Nephritis and other renal diseases, the appearance is that of loosely arrayed tubules (Datsis, 1972a). It is suggested that the several observations may all concern the same structures, and that variations in appearance of the structures may be related to the packing density of the aggregates. Similar bodies have been interpreted by earlier investigators as being viral in nature (Bucciarelli *et al.*, 1967; Kim and Boatman, 1967; Lombard *et al.*, 1967). The particle size of 20 to 25 nm reported in most of these studies, however, is larger than that for the expected diameter of the nucleocapsid of the myxovirus or paramyxovirus group (Davis *et al.*, 1967; Roizman, 1972). In addition, the localization of the aggregates within the endoplasmic reticulum or in an intimate relationship to it, as seen in most cases of Lupus nephritis (Datsis, 1972a), refutes the possibility of a viral origin of these structures, since this intracellular localization has not been a feature of either myxovirus or paramyxovirus infections, in which the virus is found either free in the cytoplasm or within the nuclei.

The biological existance of systems of undulating tubules having organized or unorganized orientations was reported by Chandra (1968). In the present investigation, substantial evidence for the existence of mutually perpendicular systems of undulating tubules was provided. Since many other orientations of

Fig. 1. Electron micrograph illustrating part of two glomerular capillaries. There is a fusion of the foot processes so that the basement membrane is covered by a thin sheet of epithelial cytoplasm. There does not appear to be any widespread capillary basement membrane thickening. The endothelium of the upper capillary contains aggregates of small round bodies arranged in a crystalline pattern (arrow). A single, smooth membrane, displaying points of an apparent continuity with the ergastoplasmic membranes is seen delimiting the endothelial inclusion. Fixation in 1% s-collidine buffered OsO_4; stained with uranyl acetate and lead hydroxide. ×22460. *CAP* capillary, *END* endothelium, *EP* epithelium, *N* nucleus, *RBC* erythrocyte.—Inset. High magnification of a section through an endothelial "inclusion" showing the tubular nature of the sub-units of the complex. Round profiles formed by undulating tubules, and displaying "hollow cores" are quite prominent (arrows). Elements of endoplasmic reticulum appear to be continuous with the array of the tubular structure. Fixation as in Fig. 1. × 32490. *TC* tubular complex

the tubules are possible (Datsis, 1972d), various images can be observed in ultrastructural studies. It is quite obvious that the most frequently observed images would be the round bodies or profiles. In an organized state, the tubules could produce images exhibiting a crystalline or tubular pattern. The round bodies, cannot, therefore, be conceived as viral in nature.

The unique appearance of the aggregates and their distribution within the endoplasmic reticulum of endothelial cells, suggest that the particles, though described in a variety of conditions, may represent a common cellular response to a variety of pathologic processes.

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