DEPOSITION OF SILICA IN MITOCHONDRIA: AN ELECTRON MICROSCOPIC STUDY

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The intraperitoneal injection of silica-gel into rats (30 to 40 mg. of silica per rat of 200 *g*) produces a nephrotic syndrome. Amongst the pathological characteristics of this syndrome are an epithelial degeneration in the proximal part of the nephron and an increase of the silica content of the whole kidney.

In all silica-treated animals, pronounced lesions of the urinary tubule with degenerated and swollen cytoplasm are visible under the light microscope. The lesions are not definitive. After about a week a new epithelium regenerates and the urinary tubules are cleaned.

Three days after the injection, the mitochondria in the proximal part of many nephrons are swollen and show less closely spaced cristae. In some mitochondria very small granulations appear which are very dense, approximately spherical, about 40 to 50 A in diameter (Fig. 1). These small particles aggregate between mitochondrial cristae, directly or with material of intermediate density, presumably proteins, and form curious electron-dense bodies, 150 to 1200 A in diameter. Frequently, in the center of these bodies there is a lighter area where the small dense particles are less numerous (Fig. 2).

In the present study the fine structure and the behavior of these formations were examined by electron microscopy with special attention to their mechanism of formation and further development.

It has been postulated that these formations are siliceous in nature for the following reasons:

(*a*) Presence only in silica nephrosis, when the silica content of the whole kidney is high (silica content in one whole normal kidney: 0.010 to 0.015 mg.; in a nephrotic kidney: 1 to 1.5 mg.).

(*b*) By microincineration, the ashes of sections are plentiful and not soluble in an HCl solution.

(*c*) Negative reaction for calcium (von Kóssa) in histological sections.

The mechanism of deposition of granules in mitochondria seems primarily and fundamentally to be a matter of diffusion of oligomeric silica molecules through the mitochondrial membranes and of polymerization of these molecules within mitochondria. Silica then becomes visible with the electron microscope in the shape of very fine dense granules, sometimes isolated but more often agglutinated.

In no case, are holes in the mitochondria membranes perceptible. Likewise there are no invaginations of the outer mitochondrial membrane. In conclusion, it may be suggested that silica penetrates into mitochondria in a diffusible form, probably oligomeric.

FIGURES 1 and 2

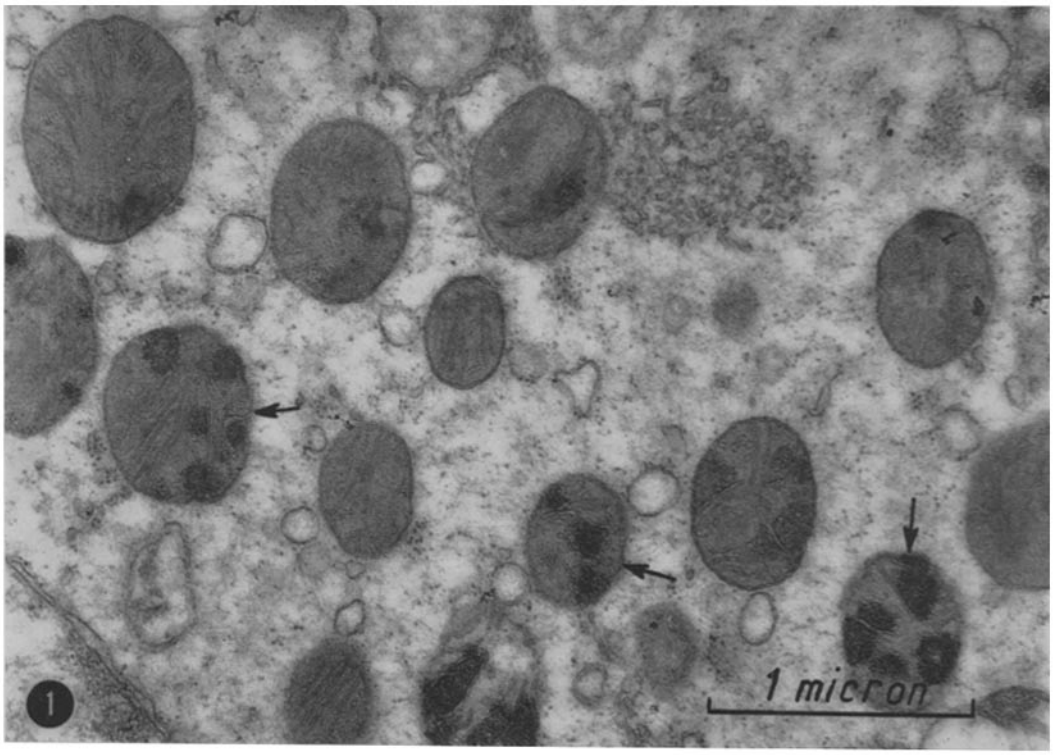
Aspects of silica deposits in mitochondria. Proximal convoluted epithelial cells of rat kidney, 18 hours after intraperitoneal injection of gelatinous silica.

FIGURE 1

First appearance of dense intramitochondrial deposits (silica) in a portion of mitochondria (arrows).

FIGURE 2

Detail of deposits in two modified mitochondria. The mitochondrion on the left is swollen, with thinned contents and modified cristae. The mitochondrion on the right remains dense but the cristae have almost disappeared.



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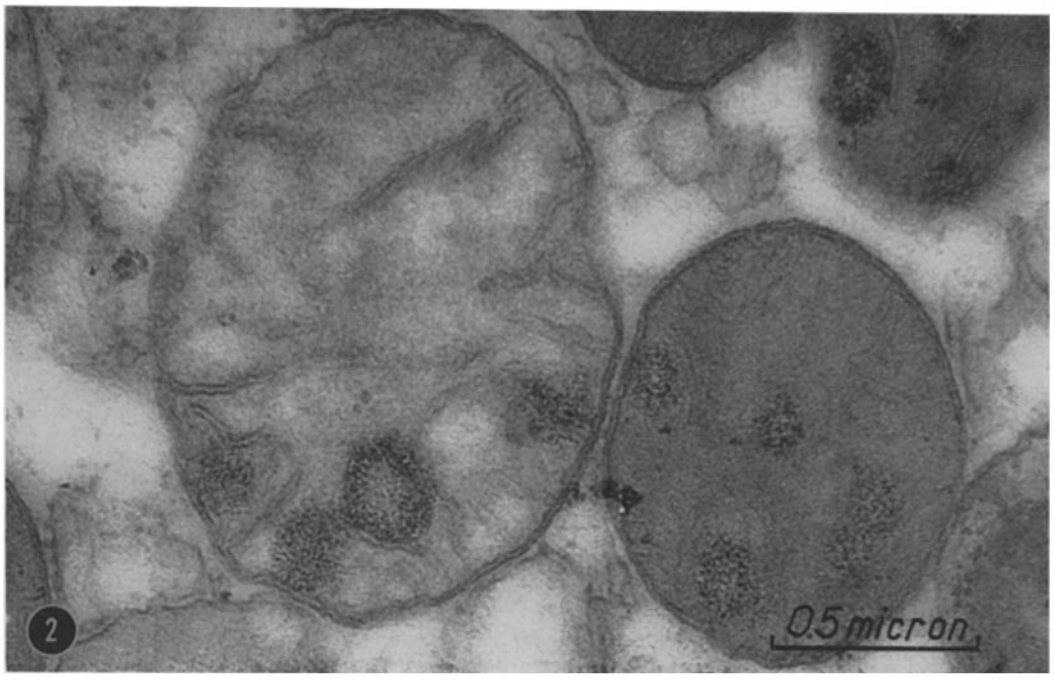

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The fate of the siliceous bodies is easily followed. By progressive swelling, the mitochondria break up, the siliceous bodies being freed in the degenerating cytoplasm. With the latter they proceed to the lumina of the urinary tubule into the casts, with which they are finally eliminated. After 2 days, when the siliceous bodies begin to appear in the necrotic substance of the casts, the silica content of the whole kidney becomes nearly normal.

Recently, the electron microscope has provided us with a means of detecting intramitochondrial deposits following silver (Dempsey, 1955) or iron (ferritin, Bessis, 1959) treatment. These deposits are situated between the cristae.

At present, it would seem that it is the same thing in the case of silica.

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