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Fine Structural Changes in Human Lead Encephalopathy

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Biopsy specimens from white matter and gray matter were removed from six children suffering from proven lead encephalopahy. The specimens were pre-fixed *in situ* and then post-fixed in osmic acid and processed for electron microscopic examination with embedding agents consisting of Epon and Vestopal W, so as to provide for examination of cellular elements and myelin sheaths. Serum lead levels and tissue levels of white matter and gray matter were also determined.

The clinical status of the patients varied from those suffering status epilepticus to those who were in deep coma and had already had at least one episode of respiratory arrest. All patients had an increase in intracranial pressure.

The fine structural changes which were noticed in the gray matter were quite different from those in the white matter. Similarly, the changes of the intracytoplasmic organelles in capillary endothelial tissue were different qualitatively and quantitatively from the gray matter to the white matter.

In the gray matter the most obvious changes noted were in the neurons. Specificially, these cells demonstrated rather consistent and noticeable distention of the lamellar components of the granular ergastoplasm, with resultant opening up, as it were, of the granular ergastoplasm. Stacking of the granular component in this organelle was also quite obvious. Changes compatible with swelling (distention of granular ergastoplasm and Golgi apparatus, plus an increase in the space intervening between the two nuclear membranes) were observed in the glial elements of the gray matter. Rupture of cell membrane and alterations in either number or size of intracytoplasmic vesicles, though observed, did not represent a very common alteration in the cells. Similarly, increase in size of the extracellular compartment, though generally present, was not very significant.

The capillary endothelium of gray matter was the site of the most obvious morphological changes. Specifically, the granular ergastoplasm of these endothelial cells demonstrated signs of severe swelling and there was rather significant increase in both number and size of intracytoplasmic vesicles. The basement membrane surrounding the capillary endothelium, and enclosing the pericytes, rather routinely took on the appearance of an amorphous mass of granular-appearing material and lost its typical triple-density aspect. The pericytes also showed signs of swelling and contained within their intracytoplasmic compartment multitudes of lipoprotein-appearing globules.

The changes in capillary endothelium in the white matter were insignificant, except in those areas where severe increase in extent of the extracellular space was noted. In these cases, however, the endothelial changes were never as obvious or consistent as in the gray matter.

The earliest and most prominent changes in the white matter were at the expense of the extracellular space, with this compartment opening up extensively in correspondence to the pericapillary area and the area intervening between glial cells, cell processes, and myelinated axons. Within the glial cells the changes were those of swelling, namely, an increase in the space intervening between the two nuclear membranes and continuity of this space with that intervening between the lamellar component of the granular ergastoplasm. The distention of the granular ergastoplasm was invariably more obvious than that noted in the Golgi apparatus. Exhaustion phenomenon of the nuclei of the glial cells was also commonly observed.

The changes within the myelin sheaths occurred at the level of the intra-period line and consisted of splitting and delamination, with resultant increase of space between two adjacent lamellae. Large vacuoles or vesicles, however, were rarely noticed. A breakdown of myelin lamellae with accumulation of electron-dense granules along the intra-period line was also commonly observed. The axonal changes consisted of a loss of neurofilaments and their replacement by diffuse granular-appearing material.