ULTRASTRUCTURAL AND BIOCHEMICAL ALTERATIONS OF CELLULAR ORGANELLES
BY PREGNATAL EXPOSURE TO TOXIC TRACE METALS

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ABSTRACT

There are relatively few studies concerning either the ultrastructural or biochemical effects of toxic elements on subcellular organelles. Ultrastructural studies which show cellular vesiculation, mitochondrial damage and cellular necrosis have been reported for lead and arsenate. Ultrastructural/biochemical data are available for the effects of methylmercury on fetal organisms. These studies show cellular vesiculation of hepatocytes, decreased synthesis of protein and DNA associated with inhibition of mitochondrial biogenesis and respiratory function. One, or a combination of these effects, appears to be responsible for the known reduction in fetal size at doses of methylmercury below which overt teratogenic or maternal toxicity are observed.

INTRODUCTION

It has been known for many years that high-dose prenatal exposure to toxic trace elements such as arsenic, cadmium, mercury, lead and indium (see review by Ferm and Hanlon, this volume) will produce gross fetal malformations. The biochemical and organelle system alterations which underly these effects have received relatively little attention and there are currently no published mechanistic data available to explain these teratogenic changes. Furthermore, there are even fewer studies involving the effects of prolonged low-dose maternal exposure to these agents on developing subcellular systems in the fetal at dose levels below which gross morphological changes occur.
The present review examines the literature pertaining to the effects of various metals on organelle systems and uses data from our laboratory to illustrate how prenatal exposure to methylmercury, at subtoxic doses in maternal rats, resulted in changes in fetal liver mitochondrial structure and biochemical function which resulted in apparent biochemical defects in this organelle later in life.

REVIEW OF LITERATURE CONCERNING SUBCELLULAR EFFECTS OF TOXIC TRACE METALS

Arsenic

Morrissey and Mottet (1983) have demonstrated a failure of closure of the rhombencephalon in fetal mice of dams injected with arsenate (45 mg/kg) on day 8 of pregnancy. They observed cell necrosis, mitochondrial damage and an increase in small, clear vesicles as prominent ultrastructural changes in neural tube cells.

Lead

DeGennaro (1978) studied the morphological effects of lead nitrate on the developing nervous system of chick embryos. By electron microscopy, he observed extensive cellular vacuolization and disorganization of the endoplasmic reticulum as most prominent early manifestations of toxicity in the central nervous system. Little morphological alteration of mitochondrial structure was observed, although biochemical dysfunction characterized by uncoupling of oxidative phosphorylation of brain mitochondria has been reported (Holtzman and Hsu, 1976) in suckling rats.

Methylmercury

Of the toxic trace elements, the in utero effects of methylmercury have been most well-studied with respect to the ultrastructural/biochemical effects of this agent in fetal and developing animals. Several studies with methylmercury (Mottet, 1974; Spyker and Spyker, 1977; Chen et al., 1979) have reported decreased birthweights and growth/development patterns in rodents exposed in utero to methylmercury. This finding is similar to that observed in infants exposed in utero to methylmercury in Iraq (Amin-Zaki et al., 1979). The underlying mechanism of this effect is not totally known but a number of studies in recent years (Fowler and Woods, 1977; Chang et al., 1977; Olson and Massaro, 1977; Robbins et al., 1978; Chen et al., 1979) have clearly demonstrated both ultrastructural and/or biochemical changes in rodents exposed