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# Maternal exposure to tributyltin alters the breast milk, hormonal profile, and thyroid morphology of dams and induces sex-specific changes in neonate rat offspring☆

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ABSTRACT

Tributyltin (TBT) is the chemical substance commonly used worldwide to prevent biofouling of vessels. Due to its ability to bioaccumulate and biomagnify, even after being banned, significant concentrations of TBT can be detected in sediment, affecting marine and human life. Although studies have shown that direct exposure to TBT alters physiological parameters in mammals, the relationship between exposure to TBT during pregnancy and lactation, considered critical windows for metabolic programming, has not been fully elucidated. Our hypothesis is that offspring whose mothers were exposed to TBT during critical stages of development may exhibit dysfunctions in endocrine-metabolic parameters. We used pregnant Wistar rats that were divided into groups and received the following treatments from gestational day 7 until the end of lactation by intragastric gavage: vehicle (ethanol 0.01%; Control), low TBT dose (100 ng/kg of body weight (bw)/day; TBT100ng) and high TBT dose (1000 ng/kg bw/day; TBT1000ng). Dams and offspring at birth and weaning (21 days old) were studied. Maternal exposure to TBT promoted dose-dependent changes in dams. The findings for adiposity, milk composition and lipid profile were more pronounced in TBT100 ng dam; however, thyroid morphology was altered in TBT1000 ng dam. Female offspring were differentially affected by the dose of exposure. At birth, females in the TBT100ng group had low body weight, lower naso-anal length (NAL), and higher plasma T4, and at weaning, females in the TBT100ng group had lower insulin and leptin levels. Females in the TBT1000ng group had lower NAL at birth and lower leptinemia and weight of white adipose tissue at weaning. Male offspring from TBT groups showed high T3 at birth, without biometric alterations at birth or weaning. Despite these findings, both sexes exhibited dose-dependent morphological changes in the thyroid gland. Thus, maternal exposure to TBT constitutes an important route of contamination for both dams and offspring.

## 1. Introduction

Marine environments are not free from contamination by substances considered endocrine disruptors, i.e., substances capable of interacting with hormonal receptors and interfering with their action and biological effects. A large quantity of contaminants from effluents, atmospheric precipitation, leaching from soil, vessels and other sources are deposited in marine ecosystems, affecting their balance. These imbalances cause

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