

## Cardiac and Aortic Function and Ultrastructure in AZT Treated FVB/n Mice

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AZT is a thymidine analog with a known efficacy against HIV-1 infection. Heart disease in AIDS is prevalent. Previous studies demonstrated AZT causes mitochondrial toxicity in cardiac and skeletal muscle of rodents. Preliminary data suggested that aortic contractility in AZT treated female mice was altered. The aim of this study is to define the effects of gender on AZT mitochondrial toxicity in aortas. The working hypothesis states that AZT alters aortic mitochondria in FVB/n female mice as compared to males. A 2x2 study used male and female mice  $\pm$  AZT (n=5 per group). Mice were given AZT (0.7mg/ml) in drinking water *ad libitum* for 5 weeks. All mice survived the duration of the experiment. Mice were sacrificed in order to obtain aortae for *ex vivo* physiologic study and tissue samples for TEM. Results showed AZT-treated females did not grow as well as their untreated counterparts (2.5 % of initial body weight vs. 10.1 % of initial body weight). AZT-treated and untreated males gained weight essentially equivalently (11.3%, 12.1 %, respectfully). Total water consumption of females was higher than the males (treated female: 202 mL; untreated female: 225 mL; treated male: 185.2 mL; untreated male: 204 mL). The average dose of the treated females was 201mg/kg/day and the average dose of the treated males was 155 mg/kg/day. *Ex vivo* studies of aortic contractility demonstrated a reduced contractile ability in only the treated higher dose female mice. One aorta from a female with 164mg/kg/day AZT and all the aortas from the treated/untreated males demonstrated normal contractility. Data suggest that the altered aortic contractility is dose dependent. Similar studies in HIV-transgenic mice will help to clarify this observation.