Elevated Blood Pressure in Offspring of Rats Exposed to Diverse Chemicals During Pregnancy

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Adverse intrauterine environments have been associated with increased risk of later cardiovascular disease and hypertension. In an animal model using diverse developmental toxicants, we measured blood pressure (BP), renal nephron endowment, renal glucocorticoid receptor (GR) gene expression, and serum aldosterone in offspring of pregnant Sprague Dawley rats exposed to dexamethasone (Dex), perfluorooctane sulfonate (PFOS), atrazine, perfluoronanoic acid (PFNA), arsenic, or nicotine. BP was assessed by tail cuff photoplethysmography, nephron endowment by confocal microscopy, and renal GR mRNA by qPCR. BP was also measured by telemetry, and corticosterone (CORT) was measured in resting or restrained Dex and atrazine offspring. Treated dams gained less weight during treatment in all groups except arsenic. There were chemical- and sex-specific effects on birth weight, but offspring body weights were similar by weaning. BP was higher in Dex, PFOS, atrazine, and PFNA male offspring by 7–10 weeks. Female offspring exhibited elevated BP at 10 weeks for PFNA and arsenic, and at 37 weeks for Dex, PFOS, and atrazine. Dex, PFOS, and atrazine offspring still exhibited elevated BP at 52–65 weeks of age; others did not. Elevated BP was associated with lower nephron counts. Dex, PFOS, and atrazine offspring had elevated renal GR gene expression. Elevations in BP were also observed in Dex and atrazine offspring by radiotomography. Atrazine offspring exhibited enhanced CORT response to restraint. Elevated offspring BP was induced by maternal exposure to toxicants. Because all treatments affected maternal gestational weight gain, maternal stress may be a common underlying factor in these observations.

Key Words: DOHaD; fetal programming; fetal physiology; maternal toxicity; maternal stress.