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Application of exposure biomarkers to determine windows of developmental susceptibility

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In this presentation, issues will be addressed surrounding the use of exposure biomarkers sampled at multiple points of time during pregnancy to determine specific time periods of susceptibility of the fetus to developmental toxicity. A case study will be discussed involving research on fetal lead exposure estimated with trimester-specific measures of lead in maternal venous blood, maternal plasma, and peripartum measures of maternal skeletal stores and analyzed in relation to offspring neurodevelopment. In this study, 1st trimester measures of maternal plasma lead were found to be superior to 1st trimester measures of maternal venous blood lead as well as 2nd and 3rd trimester measures of either plasma or venous blood lead in predicting offspring scores on the Bayley scales of mental development at 24 months of age. This may reflect the heightened vulnerability to neurotoxicants of the developing nervous system in the 1st trimester. On the other hand, in additional analyses, maternal bone lead levels were also highly predictive of infant neurodevelopment and arguably the best overall single measure, perhaps denoting the importance of cumulative maternal exposure measures in studies of fetal programming. Further insights are offered by analysis of the data using structural equation models. Exposure of the fetus to potential neurotoxicants during pregnancy must be considered as a highly dynamic process for which research using an environmental epidemiologic approach requires special attention to repeated biological marker measurements, compartmental kinetics, and novel biostatistical techniques for the approach to analyses involving multiple non-independent biological markers of exposure.