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Developmental Changes in PON1 Enzyme Activity in Young Children and Effects of PON1
Polymorphisms

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Abbreviations and Definitions:

AIC - Akaike Information Criterion

ANOVA -analysis of variance

ARE – aryl ester, specifically phenyl acetate was used in the arylesterase assay

AREase - arylesterase

CHAMACOS - Center for Health Assessment in Mothers and Children of Salinas

CI – confidence interval

CPO – chlorpyrifos-oxon

CPOase - chlorpyrifos-oxonase

CV - coefficient of variation

DZOase - diazoxonase

GEE - Generalized estimating equation

LDL - low density lipoprotein

LRT – likelihood ratio test

OP - organophosphate

PCR - polymerase chain reaction

PO - paraoxon

POase - paraoxonase

PON1 - paraoxonase 1

SNP - single nucleotide polymorphism

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Abstract

Background: Paraoxonase 1 (PON1) is an enzyme that detoxifies activated organophosphorous (OP) pesticides and is also involved in oxidative stress pathways.

Objectives: PON1 activity in newborns is lower than in adults however the ontogeny of PON1 activity is poorly characterized in young children. We examined the effects of age and *PON1* genotypes on enzyme activity in a birth cohort of Mexican-American children.

Methods: Three substrate-specific measures of PON1 activity were determined in 1143 plasma samples collected longitudinally from 458 children at five time points from birth through seven years of age. *PON1* polymorphisms at positions 192 and -108 were also genotyped in these children.

Results: Contrary to previous reports that PON1 activities plateau by age two, we observed an age-dependent increase in all three PON1 measures from birth through age seven ($p < 0.0001$).

The *PON1*₁₉₂ genotype significantly modified the effect of age on paraoxonase (POase) activity; $p < 0.0001$) such that increases in enzyme activity with age were influenced by the number of R alleles in a dose dependent manner. Children with the *PON1*_{-108CC192RR} diplotype had significantly higher mean PON1 activities and also experienced steeper increases of POase activity over time compared to children with the *PON1*_{-108TT192QQ} diplotype.

Conclusions: Lower levels of the PON1 enzyme, which is involved in protection against OPs and oxidative stress, persist in young children past age two through at least age seven. Future policies addressing pesticide exposure in children should take into account that the window of vulnerability to OPs in young children may last beyond infancy.