Early Life Exposure to Air Pollution and Diabetes in Childhood

Abby Fleisch, MD, MPH
Attending Physician, Pediatric Endocrinology and Diabetes, Maine Medical Center
Center for Outcomes Research and Evaluation, MMCRI
Assistant Professor of Pediatrics, Tufts University School of Medicine
April 30, 2018
Diabetes in Childhood

Healthy

- Insulin secretion
- Insulin action

Insulin resistance

- Insulin secretion
- Insulin resistance

Genetics, overweight
+/- environmental exposures
Diabetes in Childhood

Type 2 diabetes

Genetics, overweight +/- environmental exposures
Diabetes in Childhood

US children
~17% are obese
~9% have insulin resistance (IR)
~2-4% have hyperglycemia (HG)
~0.05% have type 2 diabetes (T2D)

~0.2% have type 1 diabetes

B-cell function (insulin secretion)

More insulin resistant  Less insulin resistant

IR
HG
T2D

Measures of Insulin Resistance

• Hyperinsulinemic euglycemic clamp
• Glucose tolerance test
  – Oral or intravenous
• Homeostatic model assessment
  – HOMA-IR: \( \frac{\text{glucose} \times \text{insulin}}{22.5} \)
• Fasting insulin
• Glucose or Hemoglobin A1c (HbA1c)
  – Beta cell secretion is insufficient for level of insulin resistance

\( \beta \)-cell function and IR
Children are not Little Adults....
Air Pollution and Insulin Resistance in Childhood

- PM$_{10}$, O$_3$, SO$_2$, NO$_2$, CO
- 10-18 year old children
- Adjusted for age, sex, and BMI

- Isfahan (n=374)
- Air pollution x 7 days
- Air pollution in upper quartile → 1.3 times odds of HOMA-IR in upper quartile

- 27 provinces (n=1413)
- Air pollution x 1 year
- In 2 of 5 regions, greater air pollution → ~ 2 times odds of ↑ fasting glucose


PM$_{10}$ 122 µg/m$^3$
Air Pollution and Insulin Resistance in Childhood

• 7-24 year olds

• Matched for age, sex, gestational age, birth weight, maternal age, education, SES
  – Children in Mexico City had higher fasting glucose (86 vs. 83 mg/dL), no difference in insulin or HOMA-IR

n=56 in Mexico City (PM$_{2.5}$ 17 µg/m$^3$)
n=26 in Polotitlan (PM$_{2.5}$ 12 µg/m$^3$)
Air Pollution and Insulin Resistance in Childhood

- $PM_{10}$, $PM_{2.5}$, $NO_2$
- Adjusted for sex, age, SES, puberty, ETS, birthweight, BMI

- 10 year olds ($n=397$)
  - Birth address
  - Per 1-SD increase in $PM_{10}$ 9% higher HOMA-IR

- 15 year olds ($n=837$)
  - Current address
  - Per 1-SD increase in $NO_2$ 6% higher HOMA-IR


Air Pollution and Insulin Resistance in Childhood

- $\text{PM}_{2.5}$, $\text{NO}_2$, $\text{NO}_x$
- 8-18 year old overweight/obese Hispanic or black children
- $n=429$ ($n=314$ with 3 year follow-up data)
  - Adjusted for age, sex, SES, ethnicity, puberty, body fat, season, time trend
  - Annual exposures → higher fasting glucose, HOMA-IR
    - 1-SD higher $\text{PM}_{2.5}$ → 27% higher HOMA-IR
  - All pollutants associated with ↓ insulin sensitivity
  - $\text{NO}_2$ associated with ↓ insulin secretion over follow-up

Air Pollution and Insulin Resistance in Childhood

- PM$_{2.5}$ and black carbon
- 6-10 year old children (n=1418)
  64% white; 68% with college-educated mothers
  - Adjusted for sex, age, race/ethnicity, maternal age, education, neighborhood household income, season, time trend
  - No association between air pollution exposure during the year or week prior and HOMA-IR

HOMA-IR Results across Studies

PM$_{10}$
122 µg/m$^3$

PM$_{2.5}$
17 µg/m$^3$

PM$_{2.5}$
15 µg/m$^3$

PM$_{2.5}$
18 µg/m$^3$

PM$_{2.5}$
12 µg/m$^3$

1.3x odds of Q4 if pollution in Q4

27% higher per SD NO$_2$

6% higher per SD PM$_{2.5}$

Magnitude of effect?

Equivalent to a 9% increase in body fat
HOMA-IR Results across Studies

Susceptible populations?

PM$_{10}$
122 µg/m$^3$

↓

1.3x odds of Q4 if pollution in Q4

PM$_{2.5}$
17 µg/m$^3$

↓

No effect modification by sex

PM$_{2.5}$
15 µg/m$^3$

↓

6% higher per SD NO$_2$

PM$_{2.5}$
18 µg/m$^3$

↓

27% higher per SD PM$_{2.5}$

PM$_{2.5}$
12 µg/m$^3$
HOMA-IR Results across Studies

- PM\textsubscript{10} 122 µg/m\textsuperscript{3}
- PM\textsubscript{2.5} 17 µg/m\textsuperscript{3} → 1.3x odds of Q4 if pollution in Q4

- PM\textsubscript{2.5} 15 µg/m\textsuperscript{3} → 6% higher per SD
- NO\textsubscript{2} 27% higher per SD

Susceptible populations?
Overweight or enriched for overweight
HOMA-IR Results across Studies

PM$_{10}$ 122 µg/m$^3$
↓
1.3x odds of Q4 if pollution in Q4

PM$_{2.5}$ 17 µg/m$^3$
↓
Stronger associations in low SES

PM$_{2.5}$ 15 µg/m$^3$
↓
Low SES

PM$_{2.5}$ 18 µg/m$^3$
↓
Susceptible populations?

PM$_{2.5}$ 12 µg/m$^3$
↓
6% higher per SD NO$_2$

27% higher per SD PM$_{2.5}$
Mediation by Obesity?

• Emerging evidence suggests an association between air pollution exposure and greater BMI z-score (or increased odds of obesity) in childhood
  

• Could this be driving the association between air pollution and HOMA-IR?
HOMA-IR Results across Studies

PM$_{10}$
122 µg/m$^3$

PM$_{2.5}$
17 µg/m$^3$

PM$_{2.5}$
15 µg/m$^3$

PM$_{2.5}$
18 µg/m$^3$

PM$_{2.5}$
12 µg/m$^3$

1.3x odds of Q4 if pollution in Q4

6% higher per SD NO$_2$

27% higher per SD PM$_{2.5}$

Adjusted for BMI

Adjusted for body fat
Prenatal Air Pollution Exposure?

• Associated with
  – Maternal glycemia
  – Low fetal growth
  – Childhood obesity

  May prime children for insulin resistance

• No association between prenatal air pollution exposure and HOMA-IR in 6-10 year olds in Boston
Type 1 Diabetes?

- Autoimmune-mediated, ↓ insulin secretion
- Type 1 diabetes has been associated with:
  - Prenatal O$_3$ and NO$_x$
  - Year prior PM$_{10}$ (but not O$_3$ or NO$_x$)
  - Lifetime O$_3$ or SO$_2$ (but not PM$_{10}$ or NO$_2$)
- Glycemic control (HgbA1c):
  - Improved with higher O$_3$ exposure
  - Not associated with PM$_{10}$ or NO$_2$
Air Pollution and Diabetes in Childhood

• Some but not all studies have shown an association of PM or NO$_2$ with insulin resistance (independent of body fat)
  – Overweight and low SES: susceptible groups?
  – No evidence for effect modification by sex

• Knowledge gaps
  – Prenatal air pollution exposure
  – Type 1 diabetes
Acknowledgements

Boston (Project Viva) collaborators

Brent Coull
Heike Gibson
Matthew Gillman
Diane Gold
Itai Kloog
Petros Koutrakis

Steven Melly
Emily Oken
Wei Perng
Sheryl Rifas-Shiman
Joel Schwartz
Antonella Zanobetti

Funding: National Institutes of Health NIDDK K12DK094721 and NIEHS K23ES024803 and the Harvard TH Chan School of Public Health.