Early Life Exposure to Air Pollution and Diabetes in Childhood

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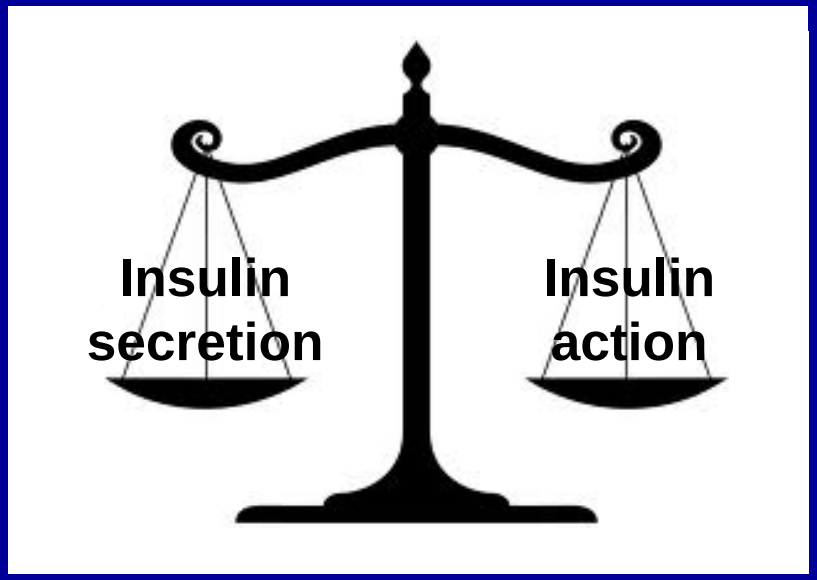
Diabetes in Childhood

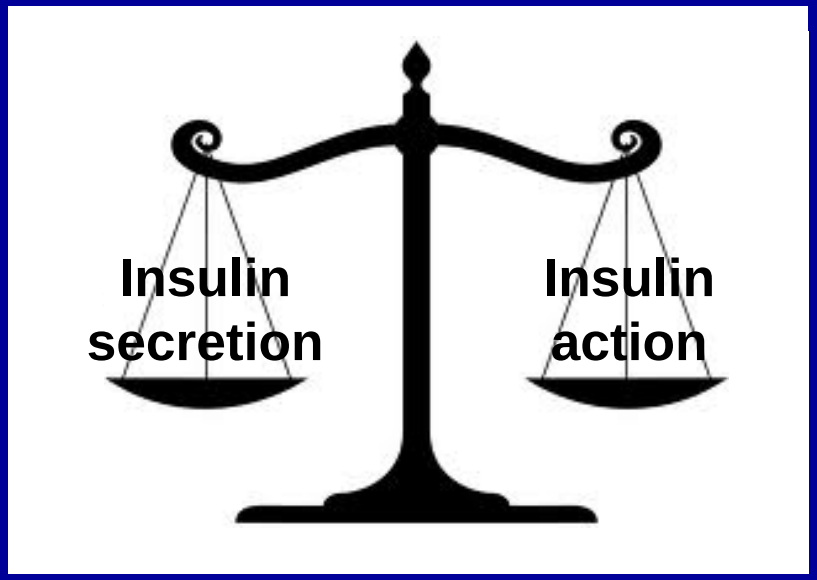
Healthy



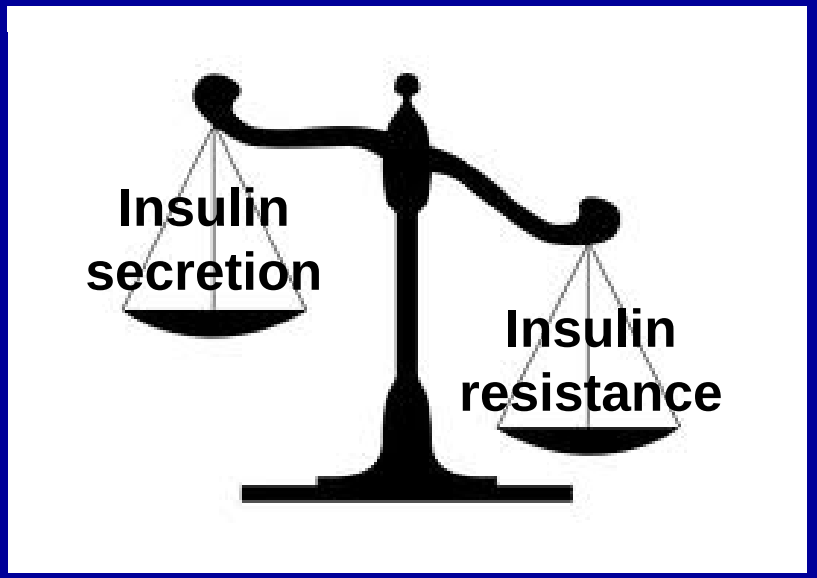
Insulin resistance

Genetics, overweight
+/- environmental exposures

Diabetes in Childhood

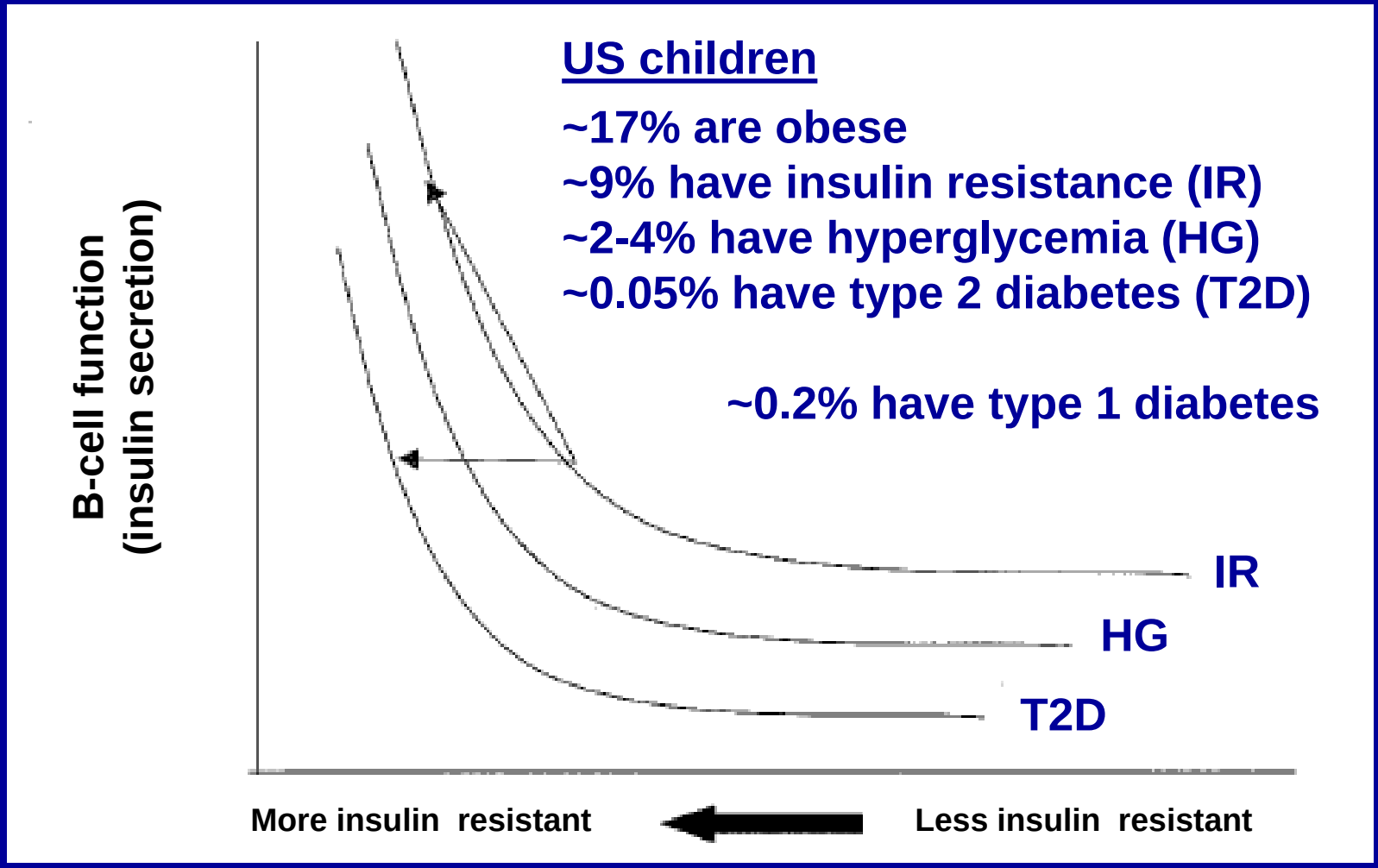


Type 2 diabetes



Genetics, overweight
+/- environmental exposures

Diabetes in Childhood



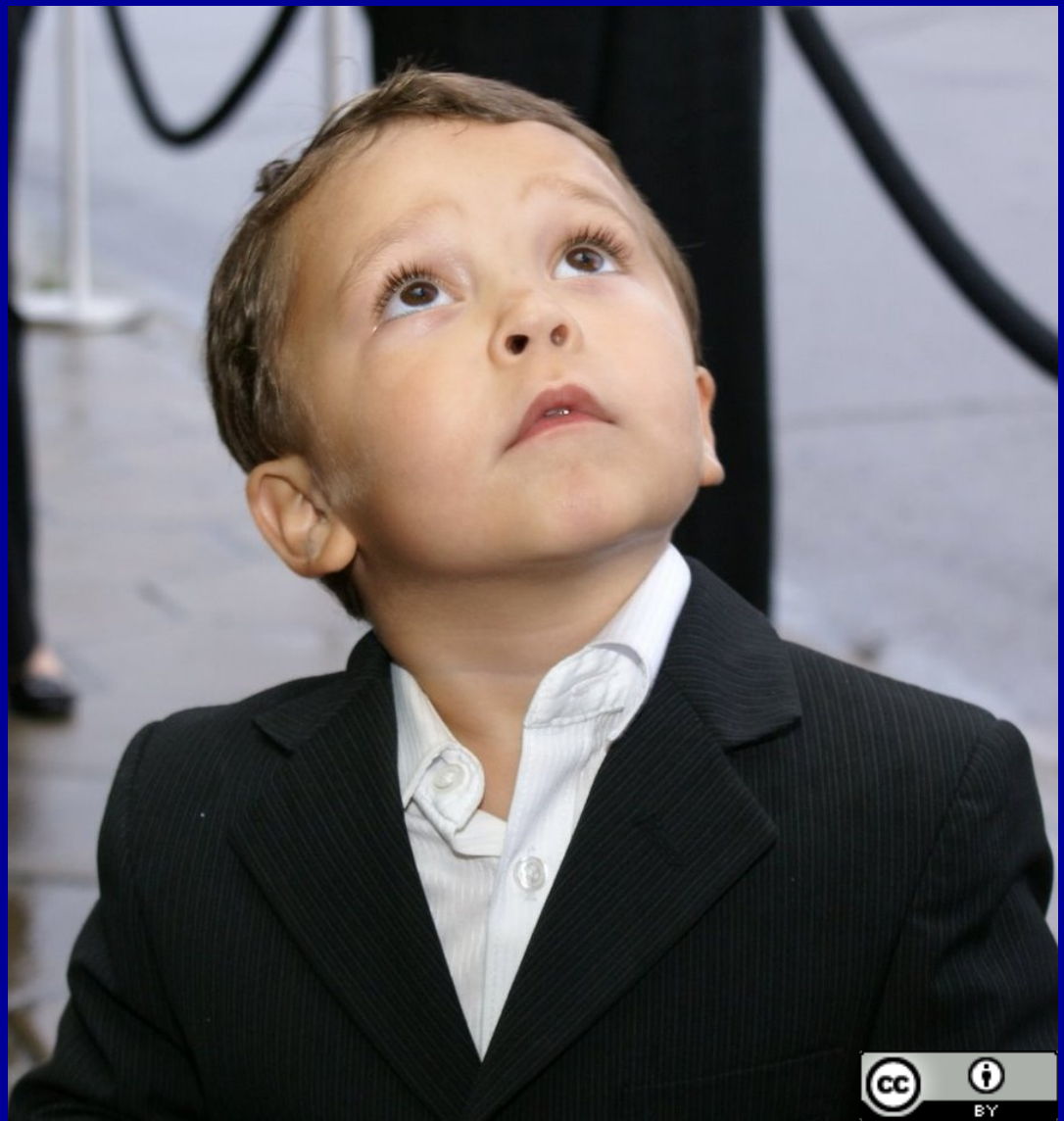
Ize-Ludlow and Sperling. Pediatric Clinics North America. 52: 1533-1552. 2005.

Measures of Insulin Resistance

- Hyperinsulinemic euglycemic clamp
- Glucose tolerance test
  - Oral or intravenous
- Homeostatic model assessment
  - HOMA-IR: (glucose x insulin)/22.5
- Fasting insulin
- Glucose or Hemoglobin A1c (HbA1c)
  - Beta cell secretion is insufficient for level of insulin resistance

β-cell function and IR

Children are not Little Adults….



Air Pollution and Insulin Resistance in Childhood

PM_{10}
122 µg/m^3

- 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

Kelishadi, et al. Atherosclerosis. 203: 311-319. 2009.

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

Poursafa, et al. Environmental Research. 134: 105-1099. 2014.

Air Pollution and Insulin Resistance in Childhood

n=56 in Mexico City ($PM_{2.5}$ 17 $\mu g/m^3$)

n=26 in Polotitlan ($PM_{2.5}$ 12 $\mu g/m^3$)

- 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

Air Pollution and Insulin Resistance in Childhood

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

$PM_{2.5}$
15 µg/m^3

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

Thiering, et al. Diabetalogia. 56: 1696-1704. 2013.

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

Thiering, et al. Environ Health Perspect. 124(8): 1291-1298. 2016.

Air Pollution and Insulin Resistance in Childhood

- $PM_{2.5}$, NO_2, NO_x
- 8-18 year old overweight/obese Hispanic or black children

$PM_{2.5}$ 18 $\mu g/m^3$

- 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 $PM_{2.5}$ → 27% higher HOMA-IR
  - All pollutants associated with ↓ insulin sensitivity
  - NO_2 associated with ↓ insulin secretion over follow-up

Alderete, et al. Diabetes. 66: 1789-1796. 2017. Toledo-Corral, et al. Pediatr Obes. 13(1): 54-62. 2018

Air Pollution and Insulin Resistance in Childhood

$PM_{2.5}$
12 µg/m^3

- $PM_{2.5}$ 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

Fleisch, et al. *Pediatric Obesity* . 12(1):48-57. 2017.

HOMA-IR Results across Studies

PM_{10}
122 µg/m³

↓

1.3x odds of Q4 if pollution in Q4

$PM_{2.5}$
17 µg/m³

↓

$PM_{2.5}$
15 µg/m³

↓

6% higher per SD NO_2

$PM_{2.5}$
18 µg/m³

↓

27% higher per SD $PM_{2.5}$

↑

Equivalent to a 9% increase in body fat

$PM_{2.5}$
12 µg/m³

↓

Magnitude of effect?

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

↓

$PM_{2.5}$
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

↓

Susceptible populations?

No effect modification by sex

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

↓

$PM_{2.5}$
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

↓

Susceptible populations?

Overweight or enriched for overweight

HOMA-IR Results across Studies

PM_{10}
122 µg/m³

1.3x odds of Q4 if pollution in Q4

$PM_{2.5}$
17 µg/m³

$PM_{2.5}$
15 µg/m³

6% higher per SD NO_2

$PM_{2.5}$
18 µg/m³

27% higher per SD $PM_{2.5}$

$PM_{2.5}$
12 µg/m³

Susceptible populations?

Stronger associations in low SES

Low SES

Mediation by Obesity?

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

Jerrett, et al. 50(1): S50-S58. 2010.
Jerrett, et al. Environ Health. 13:49. 2014
Dong, et al. Obesity. 22(3): 795-800. 2012
McConnell, et al. Environ Health Perspect. 123(4): 360-366. 2015

- Could this be driving the association between air pollution and HOMA-IR?

HOMA-IR Results across Studies

PM_{10}
122 µg/m³

↓

1.3x odds of Q4 if pollution in Q4

$PM_{2.5}$
17 µg/m³

↓

$PM_{2.5}$
15 µg/m³

↓

6% higher per SD NO_2

$PM_{2.5}$
18 µg/m³

↓

27% higher per SD $PM_{2.5}$

$PM_{2.5}$
12 µg/m³

↓

Adjusted for BMI

Adjusted for body fat

Prenatal Air Pollution Exposure?

- Associated with
  - Maternal glycemia
    Fleisch, et al. *Environ Health Perspect* 2014; 122(4):378-83
    Fleisch, et al. *Environ Health.* 2016; 15(1):40.
  - Low fetal growth
    Fleisch, et al. *Epidemiology* 2015; 26(1):43-50
  - Childhood obesity
    Chiu, et al. Environmental Research. 2017; 158: 798-805
    Mao, et al. Environ Health Perspect. 2017

May prime children for insulin resistance

- No association between prenatal air pollution exposure and HOMA-IR in 6-10 year olds in Boston Fleisch, et al. *Pediatric Obesity* . 12(1):48-57. 2017.

Type 1 Diabetes?

- Autoimmune-mediated, ↓ insulin secretion
- Type 1 diabetes has been associated with:
  - Prenatal O_3 and NO_x
    Malmqvist, et al. *Environ Res.* 2015; 140:268-274
  - Year prior PM_{10} (but not O_3 or NO_x)
    DiCiaula, et al. *Diab Res and Clin Prac.* 2016; 111:36-43
  - Lifetime O_3 or SO_2 (but not PM_{10} or NO_2)
    Hathut, et al. *Pediatr Diab.* 2006; 7:81-87
- Glycemic control (HgbA1c):
  - Improved with higher O_3 exposure
  - Not associated with PM_{10} or NO_2

    Lanzinger, et al. Diabetalogia. 2017; 158: 798-805
    Tamayo, et al. Int J Hygiene and Environ Health. 2016; 219:349-355

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

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