

# Human Health Effects of Pesticides A Pediatric Emphasis

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# Health Effects

- Acute Poisoning well described
  - Pioneering work by Wayland J. Hayes, MD
  - Not on our agenda today
- Chronic effects in Childhood
  - Little known
- Effects on the Fetus
  - Topic of today

# Chlorpyrifos

- Major, domestic insecticide until 2001
- Poor, urban dwellers had highest exposure because of crowding and poor sanitation
- Studies were mostly in New York City among Dominican and African American communities

# Effects of Prenatal Chlorpyrifos and Diazinon

- Based on cord blood pesticide assay, there was a dose dependent, statistically significant, association resulting in:
- Lowering of birth weight
- Lowering of birth length

Whyatt, Env Hlth Persp 112; 2004; 1125

# Chlorpyrifos & Diazinon

- The effects of the pesticides on fetal growth stopped when chlorpyrifos was removed from sale for domestic use.
- The use of pesticides, reported by the mothers in the study, did not change. Only the agents changed.
- Therefore, cessation stopped the effect

# Chlorpyrifos & Diazinon

- Further studies of socio-economic and cultural attributes of the study populations have failed to find any unaccounted for confounders.
- IQ and other developmental measures done in follow up have not yet been published.

# Chlorpyrifos

## Berkowitz et al.

- Found an effect on head circumference when the mothers were tested for Paraoxonase.
- Only those with PON1 had infants with reduced head circumference.

Berkowitz Env Hlth Pers 112; 2004; 388

# ATRAZINE

## Background

Used to control weeds in crops

- Allows better yields
- Prevents plowing for weed control and, thus, less soil erosion
- Cheap and easily applied
  - A valuable aid to farming
  - Its benefit has led to widespread use
  - Its now found in almost everyone in the US population!



# Human Health Effects of Atrazine

- Some potential side effects
- EPA staff to evaluate its potential cancer and non-cancer effects on humans – including potential association with birth defects, low birth weight & premature births.
- Then, it was associated with IUGR in Iowa, 1984-1990 and gastroschisis in England in 1995

# lowa contaminated water studies (EnvHlthPersp 105;1997;308)

- A county was found with high levels of triazine herbicides in the water
- The rate of IUGR, prematurity, and low birth weight were analyzed in comparison to other southern Iowa counties
- Atrazine, metolachlor, and cyanazine all were significant predictors of IUGR with atrazine the strongest

# Gastroschisis

- Failure of the embryo to fully close the abdominal wall during organ formation
- The intestines may not be fully formed and may not be patent.
- Rarely found with other congenital malformations
- Doesn't run in families.

# Gastroschesis (2)

- Surgical repair is multi-staged, costly, difficult
- Total parenteral nutrition (\$1000/d) is essential for months in many cases.
- Very severe cases (about 5 %) need total gut transplantation---only 50% survive to 20<sup>th</sup> birthday [Historically, all these infants were allowed to die in infancy]

# From an exhaustive review of gastroschesis

*'Despite the fact that large numbers of epidemiologic, clinical, and pathological studies have been performed, the etiology and developmental pathogenesis of gastroschesis has defied a rational embryological explanation'*

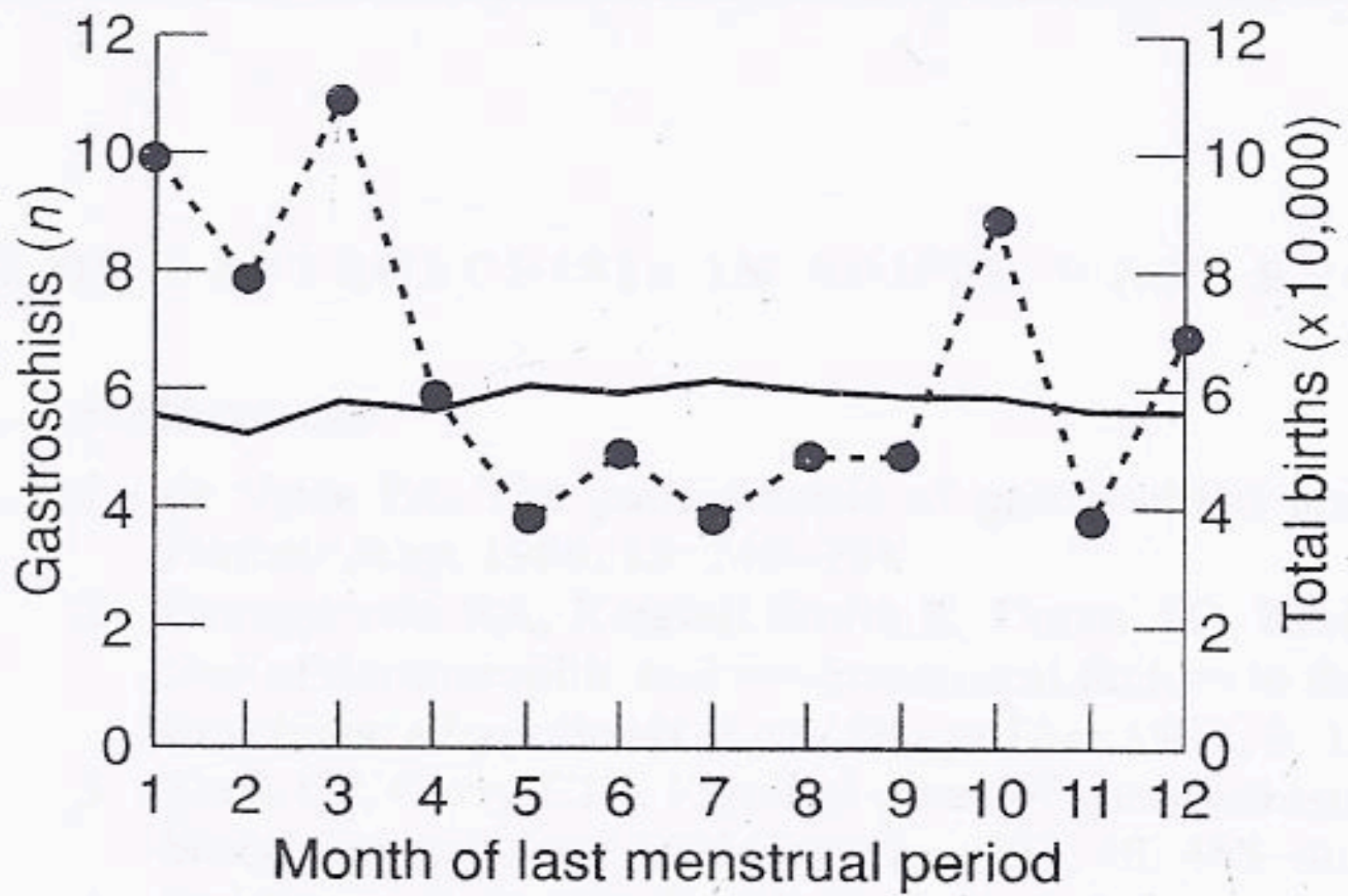
- Clin Genet 75; 2009; 322

# England in 1995

(published in 1998)

- Noted an unusual rise in incidence of gastroschisis in SW England in 1995
- Rate was highest in early teenage pregnancy but there wasn't a rise in pregnancy in this age group
- The rates were highest when the LMP was in Jan to March.

Brit J Ob Gyn 1998; 105; 328

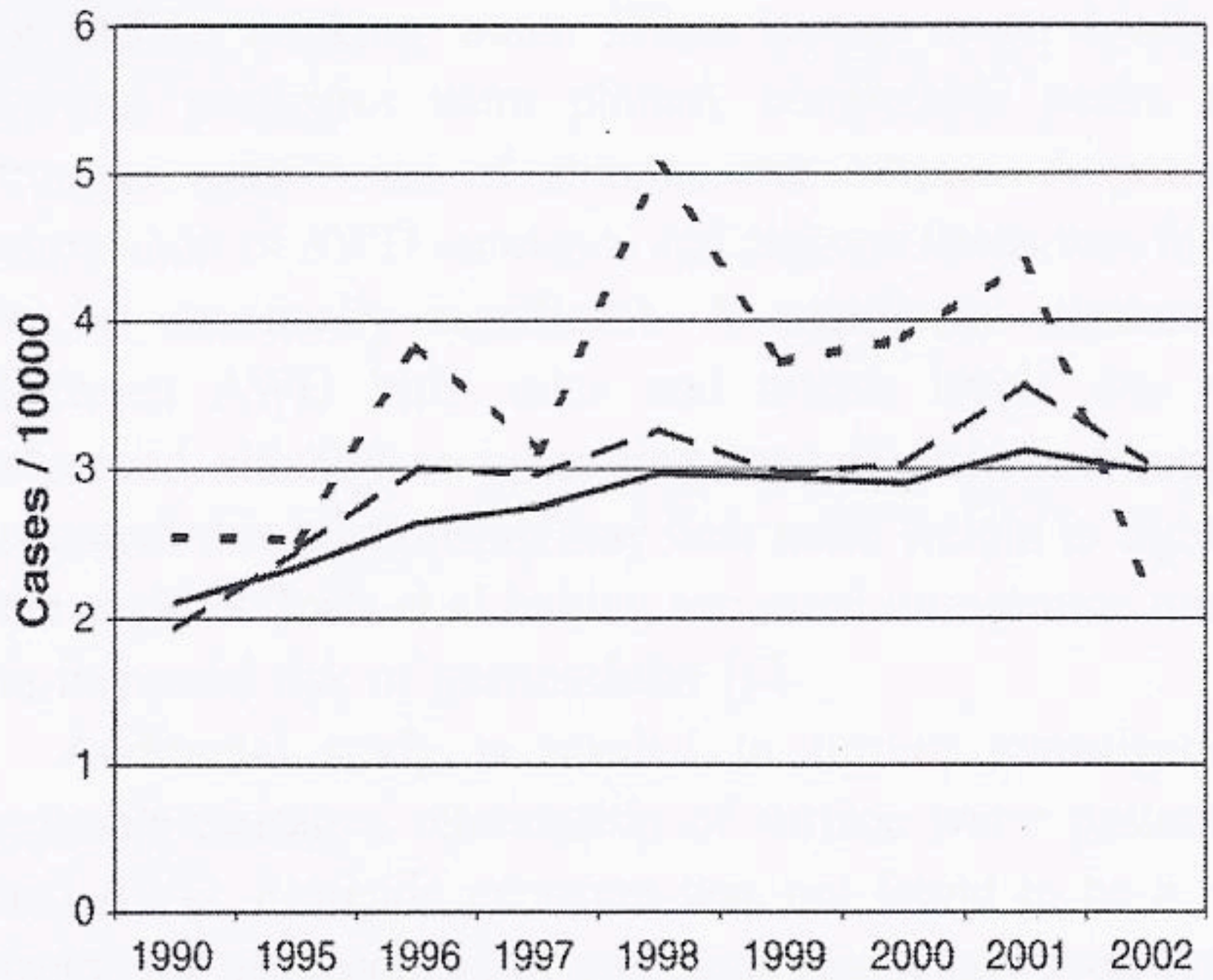


# Indiana study

(J Ped Surg 42;2007;947)

- Used Indiana and national statistics
- Incidence of gastroschisis higher in Indiana than in either similar states of the Midwest or national figures
- Peak gastroschisis rates correlated with peak environmental atrazine levels and atrazine use.





# Washington State Study

(Am J Ob Gyn 202; 2010; 241)

- Used environmental atrazine levels, location of mother's dwelling and LMP
- Atrazine levels higher than EPA exposure limit were used as a 'high dose' level
- Results:
  - More cases occurred the closer a woman lived to a locus of high atrazine level, with very high levels a particular risk
  - Cases peaked when conception occurred in months when atrazine use peaked.

TABLE 2

## Logistic regression analysis for gastroschisis development (n = 4421)

Variable	Odds ratio (95% CI)	P value
High atrazine (>3 $\mu\text{g/L}$ )		
<25 km	1.60 (1.10–2.34)	.014
25–50 km	1.41 (1.19–1.66)	<.001
>50 km	1.00 (Reference)	—

TABLE 4

**Multivariate model for spring conception  
and atrazine exposure (n = 3828)**

<b>Variable</b>	<b>Odds ratio (95% CI)</b>	<b>P value</b>
Maternal age	0.92 (0.90–0.93)	< .001
Nulliparity	1.20 (1.00–1.44)	.051
Smoking during pregnancy	1.34 (1.08–1.66)	.008
Spring conception	1.24 (1.01–1.51)	.036
Distance to high atrazine site (log)	0.80 (0.63–1.01)	.059

CI, confidence interval.

Waller. Gastroschisis risk in Washington State. *Am J Obstet Gynecol* 2010.

# Conclusions

- Gastroschesis appears correlated to atrazine with both dose and time coincidence
- There is animal data supporting the embryotoxicity of atrazine.
- I believe these studies may be refined but will not be found in error

# The Challenge

Is there a way to prevent exposure to human embryos without banning atrazine?