

Autism and Induction of Labor: *Talking Points for the Obstetrician*

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Your clinic: G1, 38 weeks

- You:

"Your blood pressure is high, and it is time to have a baby. We need to induce your labor."

- Your patient:

"OK...but I don't want pitocin."

Your clinic: G1, 38 weeks

- You:

"Pitocin is how we induce your labor."

- Your patient:

"I don't want any pitocin.

I don't want my kid to have autism."

Your clinic: G1, 38 weeks

- You:

...try to conjour a brief, compelling,
evidence-based answer....

And say, *"Pitocin doesn't cause autism."*

Your clinic: G1, 38 weeks

- You, after further thought:

"Your preeclampsia is a lot more serious than a theoretic risk of autism."

- Your patient:

"I don't want any pitocin."

Objectives

- What is autism?
- How often does it occur?
- What causes it?
- What doesn't cause it?

Objectives



**HOW DO YOU TALK TO A PATIENT
ABOUT AUTISM RISK?**

Where is this coming from?

Induced Labor Linked to Raised Risk of Autism, Study Suggests

Male children seem to be most vulnerable, researchers report


WebMD News from HealthDay

WebMD News Archive

By Denise Mann
HealthDay Reporter

MONDAY, Aug. 12, 2013
women may raise a boy, a new study suggests, including those who have

AUTISM SPEAKS®

WALK WITH US  DONATE 

Induced Labor Linked to Higher Autism Risk

Induced significantly in children whose mothers gave birth before labor, a study of more than 600,000 births showed.

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Inducing Labor Could Hurt Your Baby More Than You Know

August 14, 2013 at 11:57 AM

Michele Zipp   

THIS JUST IN 

Natural birth advocates often anger some over their stance on really trying to have a non-medicated birth without induction unless it's absolutely necessary. There will

Inducing labour may contribute to autism

Why babies were being induced in the first place still needs to be co...

The Associated Press Posted: Aug 13, 2013 12:01 PM ET | Last Updated: Aug 13, 2013 12:00 PM ET

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North Carolina Epidemiologic Study

Research

Original Investigation

Association of Autism With Induced or Augmented Childbirth in North Carolina Birth Record (1990-1998) and Education Research (1997-2007) Databases

Simon G. Gregory, PhD; Rebecca Anthopolos, MA; Claire E. Osgood, BS; Chad A. Grotegut, MD; Marie Lynn Miranda, PhD

- Largest epidemiologic study to date
- Published August 2013, JAMA Pediatrics

What is autism spectrum disorder?

- *A 'spectrum' of developmental disabilities*
 - Autism disorder
 - Asperger disorder
 - Pervasive developmental disorder, NOS
- 40% have intellectual disability (IQ <70)

What is the age at diagnosis?

- Age 2-3: Earliest possible diagnosis
- Age 4: Average age at diagnosis
- Age 8: Clinical gold standard
 - CDC ascertainment



How is it diagnosed?

- There is no single medical test
- Requires a detailed exam by a qualified professional
 - Comprehensive psychologic & behavioral eval
 - Clinical and parental observation
 - Speech and language assessment

Autism Prevalence: U.S.

1 in 68

CDC ADDM Network, 2010

Autism Prevalence: UTAH

1 in 54

CDC ADDM Network, 2010

Autism Prevalence



Number of 8-year-olds with ASDs



Total number of 8-year-olds



PREVALENCE

Autism Prevalence

**Increased 120%
between 2002-2010**

CDC ADDM Network, 2010

Autism Prevalence

- **Explanation is multi-factorial**
 - **Changes in case ascertainment**
 - **Legitimate increase in prevalence?**

Autism Prevalence

- **Boys affected 4-5 x as often as girls**
 - Consistent epidemiologic finding
 - Reasons are unclear
 - Diagnostic bias
 - Female protective effect
 - Need to stratify analyses by sex

A child with ASD might:

- Not respond by name by 12 mo.
- Not point at objects with interest by 14 mo.
- Not play “pretend” by 18 mo.
- Avoid eye contact and prefer to be alone
- Have trouble understanding feelings
- Have delayed speech and language

A child with ASD might:

- Repeat words and phrases over and over
- Get upset by minor changes in routine
- Have obsessive interests
- Do hand-flapping, spinning in circles, rocking
- Have unusual reactions to the way things look, sound, taste, or feel

What doesn't cause it?

- **Vaccinations (MMR)**
 - Immune system compromise / autoimmune rxn
 - Mercury-based preservatives (thimerosal)
 - Soundly refuted by medical research
 - >20 peer-reviewed negative epidemiologic studies
 - Dr. Wakefield's original 1998 study discredited (falsified data)

What causes it?

Genetic Risk

+

Environmental Risk

Prenatal Risk Factors

Risk Factor	Adjusted Effect Estimate
Male fetus	4 - 5
Advanced maternal age (>35)	1.6 (1.3-2.0)
Advanced paternal age (>35)	1.3 (1.2-1.5)
Parity (first vs. ≥ 3)	1.6 (1.4-1.8)
Antepartum bleeding	1.8 (1.1-2.9)
Preeclampsia	1.7 (1.3-2.3)
Diabetes	2.1 (1.2-3.5)

Modified from Guinchat, V., et al. (2012) "Pre-, peri- and neonatal risk factors for autism." Acta Obstet Gynecol Scand.

Perinatal Risk Factors

Risk Factor	Adjusted Effect Estimate
Prematurity	
<37 weeks	2.2 (1.5-3.5)
<28 weeks	2.8 (1.6-3.9)
Breech presentation	2.1 (1.1-4.0)
Cesarean delivery	
All indications	1.6 (1.1-2.3)
Scheduled	1.8 (1.3-2.5)
Fetal distress	1.5 (1.1-2.1)

Modified from Guinchat, V., et al. (2012) "Pre-, peri- and neonatal risk factors for autism." Acta Obstet Gynecol Scand.

Neonatal Risk Factors

Risk Factor	Adjusted Effect Estimate
Small for gestational age	2.1 (1.1-3.9)
Low 5 minute Apgar	3.2 (1.2-8.2)
NICU transfer	1.8 (1.3-2.7)
Neonatal encephalopathy	5.6 (2.3-13.5)
Birth defects	1.9 (1.1-3.5)

Modified from Guinchat, V., et al. (2012) "Pre-, peri- and neonatal risk factors for autism." Acta Obstet Gynecol Scand.

Oxytocin and ASD

- Role for endogenous oxytocin in normal human social and behavioral development
- Functional oxytocin deficiency and a faulty oxytocin signaling pathway have been observed in some studies of ASD
- *Does synthetic oxytocin used for labor induction alter fetal oxytocin receptors and predispose offspring to ASD?*

Induction of Labor and ASD

Leading up to 2013...

- 3 studies that showed weak association
 - Of these, only 1 showed a persistent association after controlling for confounders
- 6 studies that didn't
- All limited by small size and methodology

Gardener et al. "Prenatal risk factors for autism: comprehensive meta-analysis." Br J Psychiatry 2009

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■ Association with ASD

- Induced / augmented: OR 1.27 (1.01-1.52)
- Induced only: OR 1.13 (1.04-1.22)
- Augmented only: OR 1.16 (1.07-1.25)

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■ Association with ASD: **MALES**

- Induced / augmented: OR 1.35 (1.1-1.66)
- Induced only: OR 1.18 (1.08-1.3)
- Augmented only: OR 1.15 (1.05-1.25)

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■ Association with ASD: FEMALE

- Induced / augmented: OR 1.01 (0.67-1.53)
- Induced only: OR 0.95 (0.8-1.13)
- Augmented only: OR 1.18 (1.02-1.36)

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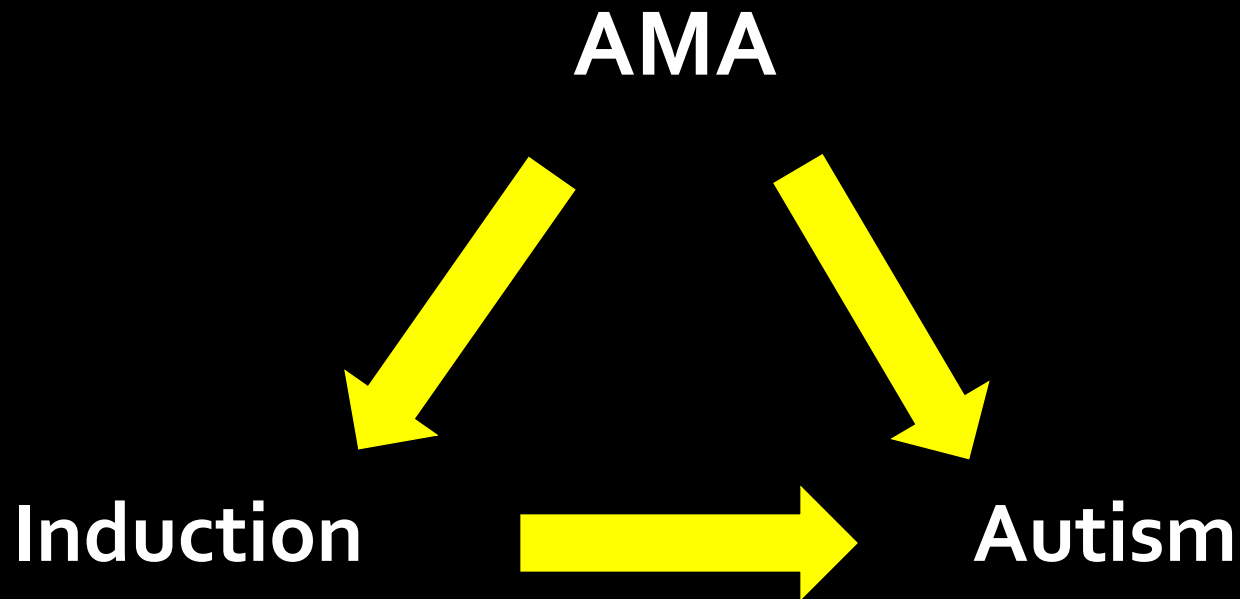
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- **Highly criticized:**
 - **Exposure data came from birth certificates**
(Induction/augmentation agent was not known)
 - **Limited ability to control for confounders**

Confounding in Autism Research

- AMA ↑ autism
- AMA ↑ induction of labor
- If you don't account for maternal age in analyses, it may look like induction of labor is associated with autism

Confounding in Autism Research



Response from SMFM / ACOG

- **SMFM Statement, 2014**
“Labor Induction or Augmentation and Autism Spectrum Disorders”
- **ACOG Committee Opinion #597, May 2014**
“Labor Induction or Augmentation and Autism”

Response from SMFM / ACOG



The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

COMMITTEE OPINION

Number 597 • May 2014

Committee on Obstetric Practice

The Society for Maternal-Fetal Medicine endorses this document. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

"...current evidence does not identify a causal relationship between labor induction or augmentation in general, or oxytocin labor induction specifically, and autism or ASD."

Response from SMFM / ACOG

"Recognizing the limitations of available study design, conflicting data, and the potential consequences of limiting labor induction and augmentation, the Committee on Obstetric Practice recommends against a change in current guidance regarding counseling and indications for and methods of labor induction and augmentation."

Utah Data – SMFM 2015

- Epidemiologic analysis using
 - Utah Registry of Autism and Developmental Disabilities (URADD)
 - Utah Department of Education
 - Utah Department of Health Vital Statistics
- 2,266 ASD cases
- 151,845 controls

Utah Data – SMFM 2015

Table. Association between labor induction and/or augmentation and autism spectrum disorder in a Utah cohort

Variable	Odds <u>ratio</u> ^a	95% CI	<u>p</u>
Induction/augmentation	Entire <u>sample</u>^b (<u>n</u> _{cases} = 2266, <u>n</u> _{controls} = 151,845)		
Not induced and not augmented	1 [REFERENCE]		
Induced and augmented	0.887	0.740-1.063	0.19
Induced only	0.973	0.875-1.083	0.62
Augmented only	0.980	0.869-1.105	0.74

Controlled for socioeconomic status, maternal health, pregnancy-related events and conditions, and birth year.

Utah Data – SMFM 2015

- Induction and/or augmentation during childbirth are not associated with increased odds of ASD in childhood in a large Utah cohort
- Results were not different for males vs. females

Summary

- U.S. incidence of autism is now 1 in 68
- Environmental and genetic risk factors both contribute to risk
- Perinatal risk factors have been identified
- Best available research shows no link between autism & induction/augmentation
 - Careful discussions of induction risk/benefit needed

Your clinic: G1, 38 weeks

- The best available research shows no link between induction of labor and autism.
- We should not avoid induction of labor, or Pitocin, when it is medically indicated.
- To do so may increase your risk of cesarean, and could put you and your baby at increased risk.