

# **Case-Control Study of Hemifacial Microsomia: Preliminary Findings**

**Martha M. Werler, Jane E. Sheehan,  
Catherine Hayes, John B. Mulliken,  
and Allen A. Mitchell**

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# Multicenter Study

**MA: Children's Hosp., Boston  
Baystate Med Ctr, Springfield**

**NY: Buffalo Children's Hosp.**

**NJ: The Cooper Health System**

**PA: Children's Hosp. of Philadelphia**

**MD: Johns Hopkins, Baltimore**

**VA: Children's Hospital of King's  
Daughters, Norfolk**

**NC: University of North Carolina  
Hosps, Chapel Hill**

**SC: Medical University of S.C.**

**GA: Children's Healthcare of Atlanta**

**MI: Children's Hosp. of MI., Detroit**

**OH: Children Hosp & Med Ctr, Akron  
Plastics & Reconst. Surgeons,  
Akron  
Children's Hosp. of Columbus**

**IN: James W. Riley Hosp. for  
Children, Indianapolis**

**WI: Children's Hosp. of WI, Milwauk.**

**IA: University of Iowa, Iowa City**

**MO: Saint Louis Children's Hosp.**

**LA: Children's Hosp. of New Orleans  
Ochsner Foundation Hosp., N.O.**

**AZ: Saint Joseph's Med Ctr, Phoenix  
Southwest Craniofacial Ctr,  
Phoenix**

**TX: Texas Children's Hosp., Houston  
Children's Medical Ctr, Dallas**

**CA: Children's Hosp. of L.A.**

**WA: Children's Hosp & Med Ctr,  
Seattle**

**CAN.: Hosp. for Sick Children, Toron.  
Alberta Children's Hosp, Calgary**

# Methods

**Cases:** HFM or unilateral an/microtia,  
excluding known inherited or  
chromosomal anomaly

**Controls:** matched to cases by age  
and pediatrician

# Methods

## Mothers interviewed:

- by telephone
- by nurse interviewer
- $\leq 3$  years after the child's birth

# Methods

**Mothers interviewed about pregnancy:**

- **demographic factors**
- **reproductive factors**
- **illnesses and medications**
- **alcohol intake, smoking**
- **diet**

# Study Hypotheses

- 1) **Vascular disruption:**  
Does vasoactive exposure increase risk of HFM?
- 2) **Abnormality of neural crest cells:**  
Does exposure to agents that affect cranial neural crest cells increase risk of HFM?

# Preliminary Findings

**Data collection: 9/1998 - 12/2002**

**As of March, 2002:**

- **251 Cases**
- **729 Controls**



# Preliminary Analysis

- **Birth characteristics**
  - birth weight, sex, twinning
- **Demographic factors**
  - maternal age, education, race,
  - family income
- **Reproductive factors**
  - pregnancy planning, parity,  
body mass

# Infant characteristics (%)

Birth weight (g)	Cases	Controls	OR
< 1500	2	<1	17.4*
1500-1999	5	1	6.8*
2000-2499	9	3	4.3*
2500-2999	26	15	2.5*
3000-3499	30	38	1.1
3500-3999	21	34	Ref.
>4000	8	9	1.2

\*  $p < 0.05$

## Infant characteristics (%)

<b>Sex</b>	<b>Cases</b>	<b>Controls</b>	<b>OR</b>
male	58	52	1.3
female	42	48	Ref.

## Infant characteristics (%)

<b>Number of gestations</b>	<b>Cases</b>	<b>Controls</b>	<b>OR</b>
singleton	<b>93</b>	<b>98</b>	<b>Ref.</b>
<b>≥ twin</b>	<b>7</b>	<b>2</b>	<b>4.0*</b>

\*  $p < 0.05$

# Multiple Gestations

<b>Characteristic</b>	<b>Cases N=17</b>	<b>Controls N=13</b>
fetal death	<b>4 (24%)</b>	<b>3 (23%)</b>
monozygotic	<b>2 (12%)</b>	<b>1 (8%)</b>
dizygotic	<b>11 (65%)</b>	<b>10 (77%)</b>
unknown zygosity	<b>4 (24%)</b>	<b>2 (15%)</b>
IVF	<b>6 (35%)</b>	<b>2 (15%)</b>

# Multivariate Adjusted Odds Ratio (MVOR)

For each demographic and reproductive factor:

- odds ratios were
- adjusted for the effects of other factors

## Demographic Factors (%)

<b>Mat. age</b>	<b>Cases</b>	<b>Controls</b>	<b>MVOR</b>
<20 y.o.	9	8	0.8
20-24 y.o.	19	20	0.7
25-29 y.o.	26	28	Ref.
30-34 y.o.	31	28	1.3
≥35 y.o.	14	16	1.0

# Demographic Factors (%)

<b>Maternal education</b>	<b>Cases</b>	<b>Control s</b>	<b>MVOR</b>
< 12 years	24	17	0.8
12 years	22	21	1.2
13-15 years	23	23	1.2
≥16 years	31	39	Ref.

\*p < 0.05



## Demographic Factors (%)

Race/ethnicity	Cases	Controls	MVOR
White	59	66	Ref.
Hispanic	30	17	1.7*
Black	4	12	0.4*
Asian	4	4	1.1
Native American	3	1	3.3*

\*  $p < 0.05$

# Demographic Factors (%)

Income	Cases	Control s	MVOR
< \$15,000	14	12	1.8
\$15- 25,000	18	12	2.2*
\$25- 35,000	9	12	0.9
\$35- 65,000	20	26	1.0
>\$65,000	26	31	Ref.

# Reproductive Factors (%)

<b>Planned pregnancy</b>	<b>Cases</b>	<b>Controls</b>	<b>MVOR</b>
yes	58	54	Ref.
no	42	46	0.9

# Reproductive Factors (%)

When pregnancy suspected	Cases	Controls	MVOR
< 5 weeks	70	71	Ref.
5-9 weeks	21	24	0.8
> 9 weeks	9	5	1.9*

\* P < 0.05

# Reproductive Factors (%)

<b>Parity</b>	<b>Cases</b>	<b>Controls</b>	<b>MVOR</b>
primiparous	<b>70</b>	<b>71</b>	<b>Ref.</b>
multiparous			
livebirth(s)	<b>39</b>	<b>40</b>	<b>1.1</b>
fetal death(s)	<b>21</b>	<b>17</b>	<b>1.4</b>
termination(s)	<b>11</b>	<b>11</b>	<b>1.0</b>

# Reproductive Factors (%)

Pre-preg. BMI (kg/m <sup>2</sup> )	Cases	Control s	MVOR
< 19	12	6	2.1*
19-23.9	47	53	Ref.
24-27.9	17	20	0.9
28-31.9	12	11	1.3
≥ 32	8	8	0.9

\* p < 0.05

# Statistically Significant Risk Factors for HFM

- Low birth weight
- Multiple gestation
- Low socioeconomic status
- Hispanic or Native American
- Late recognition of pregnancy
- Low body mass index

# Next Steps

**Examine case subgroups:**

- **HFM “Expanded Spectrum”**  
(dermoid, coloboma, vertebral anomalies)
- **Unilateral microtia**
- **Associated defects**
  - **craniofacial**
  - **extra-craniofacial**



