

# **Military Service, Gulf War Service, and Hemifacial Microsomia**

**Martha M. Werler  
Catherine Hayes  
Jane E. Sheehan  
Allen A. Mitchell**

**Presented at  
Teratology Society  
Annual Meeting**

**Philadelphia, PA  
June 25, 2003**



**Slone**  
Epidemiology Center

# Background: Gulf War and Birth Defects

- Concerns were raised by veterans
- Potential exposures include
  - Petroleum solutions
  - Insecticides
  - Sandstorm dust
  - Arthropod-born pathogens
  - Sarin
  - Mustard gas
  - Prophylactic medications
  - Vaccines



# **Background: Gulf War and Birth Defects**

- **Several studies looking at reproductive outcomes**
- **Two large birth defect studies**
  - **Births at U.S. military hospitals after Gulf War through 10/1/93**
  - **Births in six U.S. states among active military personnel in February 1991**
- **No specific exposures were targeted**



# Background: Gulf War and Birth Defects

- ~34,000 Gulf War veterans
- ~41,000 Non-deployed veterans
- No associations were observed for:
  - Birth defects overall
  - Severe malformations
  - Genitourinary malformations
  - Heart defects
  - Hip dislocation
  - Chromosomal anomalies



# **Background: Gulf War and Birth Defects**

- **AZ, ARK, CA, GA, HI, and IA**
- **450 births to GWV mothers – too few to estimate most specific birth defect risks**
- **11,511 births to GVW fathers**
- **29,086 births to non-deployed veteran (NDV) fathers**
- **Again, no specific exposures**
- **Relative risks for 48 separate malformations**



# Background: Gulf War and Birth Defects

	<u># exp/ # unexp</u>	<u>RR (95% CI)</u>
<b>Maternal GWV</b>		
Hypospadias	4/4	6.4 (1.5-26.8)
<b>Paternal GWV</b>		
Tricuspid Vlv Atr	10/9	2.7 (1.1-6.6)
Aortic Vlv Sten	5/2	6.0 (1.2-31.0)
Coarctation	5/3	4.0 (1.0-16.8)
Renal agenesis	5/0*	16.3 (p=.011)



# Background: Gulf War and Birth Defects

	<u># exp/ # unexp</u>	<u>Adjusted RR (95% CI)</u>
<b>Maternal GWV</b>		
Hypospadias	4/4	<del>6.4 (1.5-26.8)</del>
<b>Paternal GWV</b>		
Tricuspid Vlv Atr	10/9	<del>2.7 (1.1-6.6)</del>
Aort Vlv Sten	5/2	<del>6.0 (1.2-31.0)</del>
Coarctation	5/3	<div data-bbox="1268 1312 1390 1435" data-label="Image"></div> 4.0 (1.0-16.8)
Renal agenesis	5/0*	16.3 (p=.011)



# **Background: Gulf War and Birth Defects**

- **Particular concern raised about Goldenhar syndrome – case reports**
- **Followed by reports in newspapers, on television, and the Web**
  - **Search for “Gulf War” and Goldenhar**
  - **131 hits**

# **Background: Gulf War and Goldenhar Syndrome**

- **~34,000 GWVs**
- **~41,000 non-deployed veteran (NDV)**
- **Medical record reviews to identify possible cases**
- **Cases had**
  - **anotia, microtia, or preauricular tags AND**
  - **mandibular hypoplasia OR epibulbar dermoid OR coloboma of upper eyelid**

# Background: Gulf War and Goldenhar Syndrome

	<u>GWVs</u>	<u>NDVs</u>
Goldenhar Synd.	5	2
Livebirths	34,069	41,345
Prevalence rate	14.7/100,000	4.8/100,000
	RR=3.0 (0.6-21)	

Araneta MRG et al. Teratology 1997;56:244-51

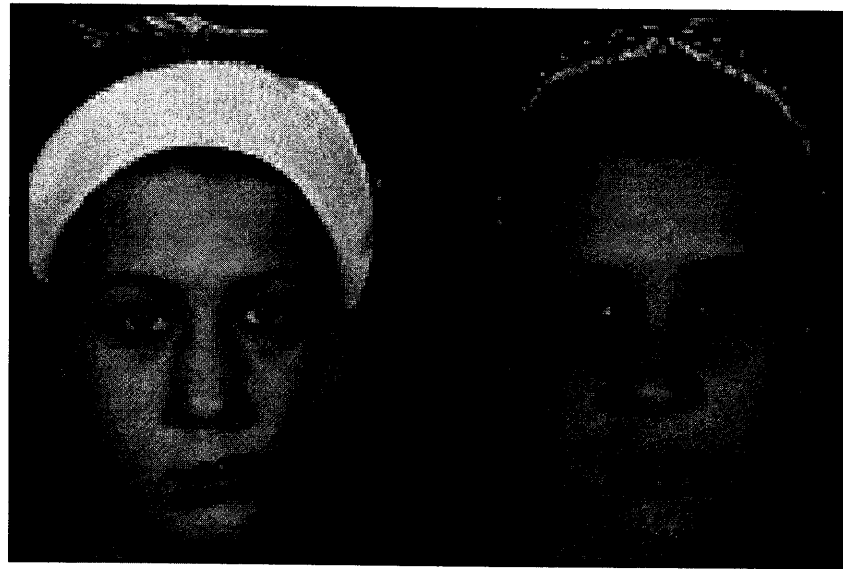


**Slone**  
Epidemiology Center

# Goldenhar vs. Hemifacial Microsomia (HFM)

- HFM is asymmetric underdevelopment of
  - Mandible
  - Ear
  - Orbit
  - Cranial nerves
  - Soft tissues
- Phenotypic variability





[www.worldcf.org/fc\\_1.html](http://www.worldcf.org/fc_1.html)



**Slone**  
Epidemiology Center

# Hemifacial Microsomia

## “Expanded Spectrum”

### –Eye

–Dermoid

–Coloboma

### –Skeletal

–Vertebral

–Limb

### –CNS

### –Cardiac

–Conotruncal

–VSDs

### –Renal

### –Gastrointestinal

### –Pulmonary

–TE Fistula

–Choanal atresia



# What is Goldenhar?

## “Expanded Spectrum”

- Eye
  - Dermoid
  - Coloboma
  - Skeletal
    - Vertebral
    - Limb
  - CNS
- Goldenhar**

- Cardiac
  - Conotruncal
  - VSDs
- Renal
- Gastrointestinal
- Pulmonary
  - TE Fistula
  - Choanal atresia



# **Hemifacial Microsomia Study**

**Objective:**

**To identify vasoactive and other risk  
factors for hemifacial microsomia  
(HFM)**



# **Hemifacial Microsomia Study**

- **1997-2002**
- **Retrospective study**
- **Multicenter study – U.S. and Canada**
- **Cases from craniofacial centers**
- **Controls from case's pediatrician's office**

# **Hemifacial Microsomia Study**

- **Cases diagnosed with**
  - Hemifacial microsomia
  - Facial asymmetry
- **< 3 years of age**

# **Hemifacial Microsomia Study**

- **239 cases**
- **854 non-malformed controls**

# **Hemifacial Microsomia Study**

- **Mothers were interviewed by telephone**
- **Questions on**
  - **Demographic factors**
  - **Reproductive factors**
  - **Behaviors**
  - **Illnesses and medications**
  - **Military service**

# **HFM Study: Demographic and Reproductive Factors**

**Race (black ↓ )**

**Income ( ↓ )**

**Multivitamin use ( ↓ )**

**Body mass index ( ↓ )**

**Alcohol intake ( ↑ )**

**Twin ( ↑ )**

**Diabetes ( ↑ )**



# **Hemifacial Microsomia Study**

**Did you serve in the military before [baby]  
was born?**

**What branch?**

**Did you serve in the Gulf War?  
(8/90-6/91)**

**When did your Gulf War service  
begin and when did it end?**

# **Hemifacial Microsomia Study**

**Did the [baby's] father serve in the military  
before [baby] was born?**

**What branch?**

**Did you serve in the Gulf War?  
(8/90-6/91)**

**When did your Gulf War service  
begin and when did it end?**



# **HFM Study: Diabetes**

- **19 Diabetic cases and 12 diabetic controls**
- **Subgroup analyses without diabetics**



# Hemifacial Microsomia

## Study: Military Service

	<u>Cases</u>	<u>Controls</u>
Maternal – any	5/239 (2.1%)	10/854 (1.2%)
- excl. diab.	5/220 (2.3%)	9/842 (1.1%)
Paternal - any	31/239(12.9%)	102/854 (11.9%)



# Hemifacial Microsomia

## Study: Military Service

	<b><u>Unadjusted OR (95% CI)</u></b>	<b><u>Adjusted OR (95% CI)</u></b>
<b>Maternal – any</b>	<b>1.8 (0.6-5.4)</b>	<b>2.2 (0.7-7.1)</b>
<b>    excl. diab.</b>	<b>1.8 (0.6-5.4)</b>	<b>2.2 (0.7-6.8)</b>
<b>Paternal - any</b>	<b>1.1 (0.7-1.7)</b>	<b>1.3 (0.8-2.1)</b>



# Hemifacial Microsomia

## Study: Gulf War Service

	<b>Cases</b> <b><u>N=239</u></b>	<b>Controls</b> <b><u>N=854</u></b>
<b>Maternal or paternal Gulf War service</b>	<b>4 (1.7%)</b>	<b>23 (2.7%)</b>



# Hemifacial Microsomia

## Study: Gulf War Service

	<b>Unadjusted <u>OR (95% CI)</u></b>	<b>Adjusted <u>OR (95% CI)</u></b>
<b>Maternal or paternal Gulf War service</b>	<b>0.6 (0.2-1.9)</b>	<b>0.8 (0.3-2.5)</b>



# Hemifacial Microsomia

## Study: Gulf War Service

	<b>Cases</b> <b><u>N=239</u></b>	<b>Controls</b> <b><u>N=854</u></b>
<b>Maternal or paternal GWV</b>		
- Army	4 (1.7%)	9 (1.1%)
- Other branch	0	14 (1.6%)



# Hemifacial Microsomia

## Study: Gulf War Service

	<b>Unadjusted <u>OR (95% CI)</u></b>	<b>Adjusted <u>OR (95% CI)</u></b>
<b>Maternal or paternal – Army GWV</b>	<b>1.7 (0.5-5.5)</b>	<b>3.2 (0.9-11.4)</b>



# Hemifacial Microsomia

## Study: Any Military Service

	Cases	Controls
<u>Maternal</u>	<u>N=239</u>	<u>N=854</u>
Army	3 (1.3%)	4 (0.5%)
Navy	1 (0.4%)	2 (0.2%)
Air Force	1 (0.4%)	1 (0.1%)
Marines	0	1 (0.1%)
National Guard	0	2 (0.2%)



# Hemifacial Microsomia

## Study: Any Military Service

<b><u>Paternal</u></b>	<b><u>Cases</u></b> <b><u>N=239</u></b>	<b><u>Controls</u></b> <b><u>N=854</u></b>
<b>Army</b>	<b>22 (9.6%)</b>	<b>42 (4.9%)</b>
<b>Navy</b>	<b>3 (1.3%)</b>	<b>24 (2.8%)</b>
<b>Air Force</b>	<b>1 (0.4%)</b>	<b>13 (1.5%)</b>
<b>Marines</b>	<b>2 (0.8%)</b>	<b>12 (1.4%)</b>
<b>National Guard</b>	<b>2 (0.8%)</b>	<b>4 (0.5%)</b>
<b>Unknown</b>	<b>1 (0.4%)</b>	





# Hemifacial Microsomia

## Study: Any Military Service

	<b>Unadjusted <u>OR (95% CI)</u></b>	<b>Adjusted <u>OR (95% CI)</u></b>
<b>Maternal or paternal - Army</b>	<b>1.9 (1.1-3.2)</b>	<b>2.3 (1.3-4.1)</b>



# **HFM Study: Conclusions**

**HFM risk is not increased for  
offspring of parents who served in  
the Gulf War six to ten years before  
the time of conception**

# **HFM Study: Conclusions**

**HFM risk is approximately doubled  
for offspring of parents who served  
in the Army branch of the U.S.  
military before conception**

# **HFM Study: Limitations**

- **Clinic-based study = incomplete  
ascertainment**
- **Imperfect measure of ‘exposure’**
  - **Service**
  - **Duties**
  - **Exposures**

# **HFM Study: Limitations**

- **6-10 years between Gulf War and conception**
- **Confounding by other factors?**