

**PARTNERS IN PERINATAL HEALTH
CONFERENCE
MAY 18, 2010**

*“Gestational Malnutrition:
Does it really exist?”*

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Gestational Malnutrition ©

does it really exist?

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Disclosures

- “No More Morning Sickness” Plume NY, 1993.
- “Take Two Crackers and Call Me in the Morning!”
[English, Spanish] 1995, 1997.
- “Morning sickness: all day & all night” (video)
Lemon Aid Productions, Woburn
- “Managing Morning Sickness: a survival guide for pregnant women”. Bull Pub. Boulder, Co. 2004

Objectives

1. Starting point: 2007 hyperemesis study
2. Pregnancy facts & stats
3. Starvation in pregnancy: then & now
4. Normal fetal development
5. Overview of 6 nutrients deficiencies
6. Observations

USC UNIVERSITY OF SOUTHERN CALIFORNIA

Symptomatology and Outcomes of Women with Hyperemesis Gravidarum as Reported in a Large Registry

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Introduction: Hyperemesis gravidarum (HG) is a severe form of nausea and vomiting of pregnancy (NVP) occurring in 1-2% of pregnant women. Our understanding of the spectrum of symptoms and outcomes of HG has been limited by small series of HG patients, giving an incomplete view of this condition.

Objective: Our objective is to report the symptomatology and severity of HG from a large registry of HG patients and to describe the clinical course of HG patients. This is the first report of a large number of affected women from an HG registry.

Methods: The National Hyperemesis Gravidarum Research (NHGR) Consortium administered an online survey from 2007-2008, capturing a wide range of clinical, symptomatology, and outcome data.

Results: The study population included 818 cases and 844 controls. Of the 818 women with HG, 40% reported having more than one symptom, 57% reported a weight loss of more than 5% of pre-pregnancy weight, 21% had 10% or more of pre-pregnancy weight loss, and 19% had 15% or more of pre-pregnancy weight loss. Weight loss of 15% (99/214, 46%) was significantly associated with:

- severe nausea
- severe vomiting
- severe dehydration
- severe electrolyte abnormalities
- severe ketonuria
- severe hypotension
- severe tachycardia
- severe hypoxia
- severe hyperthermia
- severe hypoglycemia
- severe hypocalcemia
- severe hypomagnesemia
- severe hypokalemia
- severe hyponatremia
- severe hypophosphatemia
- severe hypocalcemia
- severe hypomagnesemia
- severe hypokalemia
- severe hyponatremia
- severe hypophosphatemia

Conclusions: This study provides a comprehensive overview of the symptomatology and outcomes of HG patients. The findings suggest that HG is a severe condition that can lead to significant complications. Further research is needed to better understand the pathophysiology of HG and to develop effective treatments.

Symptomatology & Outcomes: Hyperemesis Gravidarum Registry

27th Society of Maternal
Fetal Medicine 2007

819 HG vs 541 controls

16% HG ↓ <5% wt

27% HG ↓ 5-10% wt

49% HG ↓ 10-20% wt

10% HG ↓ >20% wt

Offspring of HG with ↑
rates of behavioral,
emotional, learning
disorders vs. controls

Behavioral: 7% vs. 2.5%

Emotional: 4% vs. 1%

Learning: 4% vs. 1%

Sensory: 3% vs. 1%

Korst et al 2007 www.helpHER.org

Symptomatology & Outcomes: Hyperemesis Gravidarum Registry

Problem	HG	Controls	P value
Baby died	8	2	0.298
<2500 g	69	35	0.268
Autism	11	3	0.262
Behavioral d/o	53	9	<0.001
Birth defect	30	20	0.782
Child w/ colic	130	22	<0.001
Emotional d/o	29	4	0.007
Child w/ GERD	115	45	0.003
Learning d/o	36	4	0.001
Sensory d/o	27	3	0.006
+Inpatient Treatment	487	5	<0.001

Symptomatology & Outcomes: Hyperemesis Gravidarum Registry

- Are the problems of these children related to maternal weight loss due to hyperemesis?
- Are the problems of these children related to malnutrition- nutrient deficiencies- in pregnancy?

Sick moms ask “Will my baby be OK?”

NVP/Morning Sickness N=903
(Calif)

-N, -V
+N, -V
+N, +V

Miscarriage: 10.3% in +NVP
vs 31.7% in -NVP.

(adj odds ratio: 0.18, CI 0.06-0.53)

Weigel, Weigel 1989

Hyperemesis: Canada 1988-2002
156,091 singleton pregnancies

1270 HG's w/ 1 or more admits <
24 wks. HG babies

1. ↑ LBW (12.5% vs 4.2%)
2. ↑ < 37 wk deliveries (13.9% vs 4.9%)
3. Lower apgar scores @ 5 minutes <7

Dodds et al 2006

Fetal Origins of Adult Disease (or The Barker Hypothesis)

“... many chronic adult conditions have antecedents in compromised fetal and early prenatal development”... (1) (2)

1. Nijland et al. 2008 2. Yjnik, Deshmukh 2008

Pregnancy Facts & Stats

6.1 Million conceptions (1)
 1.3 Million TAB's (1)
 Recurrent aborters: 0.1% (2)

1 Million fetal deaths (1)
 US Births: ~3.8 Million/yr (1)

Birth defects/congenital anomalies: ~3% (~126K) (3)

Twins: 130K pairs 2003 (4)
 NVP: 50-90% preg
 HG: 1.3-2.5% (60K) (5)
 PROM: 15% (2)
 Previa: 0.5%
 Abruptions: 0.7% (2)
 Preterm labor: 12% (2)
 GDM's: 3.5% (2)
 Pre-eclampsia: 5% (2)

1. Mensereau 2. Barbieri, R. 9.16.08 3. Canfield 2006
 4. April Rudat, RD 5. Korst 2007

Neonatal Deaths..

“Some babies who are underweight for their gestational age suffer from fetal malnutrition.....

.. **fetal malnutrition** is an important **cause of death** among neonates and, furthermore, that it is most likely caused by **maternal malnutrition**”.

Metcoff J. "Biochemical markers of intrauterine malnutrition". IN. Nutrition and Fetal Development". 1974.

Theories of Congenital Anomalies

1. infections: bacterial or viral
2. birth trauma
3. genetics
4. maternal RX and/or etoh
5. in utero exposure to toxins and/or badness*
6. maternal stress (1)
7. older mother/father
8. foreign born mother (2)
9. premature birth
10. ↓ prenatal diet and/or food insecurity (3,4)
11. hypoxia during pregnancy
12. Terbutaline (1)
13. COMBO

1. Connors 2005 2. Williams 2007
 3. Susser 2008 4. Carmichael 2007

*Congenital anomalies/birth defects

- Physical: obvious @ birth
- Cognitive: not obvious @ birth
 AVOID pre-conceptual and/or in utero
 Mercury exposure.
saveJapan.Dolphins.org
Takepart.com/thecove

Dutch Famine data

October 1944 to May 1945: Nazi blockade
 <500 kcal/d. April 1945. "Tulips/food"

↑ risk of congenital anomalies of the CNS, including Neural Tube Defects and **schizophrenia** personality d/o dx'd age 18 yr in military (ie males) (1)

Susser et al. 2008

Dutch Famine impact

Defect	Timing of insult	T1	T2	T3
1. Impaired glucose		X		
2. CHD		X		
3. Atherogenic lipid profile		X		
4. ↑ Fibrinogen/↓ Factor VII		X		
5. HTN				X
6. Obstructive airway disease		X		
7. Congenital anomalies of CNS		X		
8. Schizophrenia/Sch spectrum d/o		X		
9. Anti-social personality d/o		X		
10. Affective disorders			X	X

Kyle 2006

China Hunger data

Spring 1959- early 1961. "Great Leap Forward"
 (Industrialization/famine: 30-40 million est deaths)
 "Tree bark/food".

1960-61 birth cohorts 2X ↑ rates of **schizophrenia**

Clair et al 2005

Fetal Malnutrition

1. Lack of food
2. Psychiatric
3. GI
4. Placental compromise
5. Infections
6. Multiple gestations ?
7. Hyperemesis
8. Other ??

Normal Fetal Development

Embryonic stage: fertilization to week 8
Wk 3: brain, spinal cord, heart and GI tract
Wk 4-5: limb rudiments obvious, brain develops into 5 areas
Wk 6: brain and lungs continue to form
Wk 7: all essential organs forming
Wk 8: ossification: occiput, mandible. Pleural pericardial cavity forming. Eyes, ears, nose, mouth recognizable

Normal Fetal Development

Fetal stage: week 8 to week 40
Wk 8: embryo 2.1-2.5 cm, 1 gm, head makes up ½ of the bulk. RBC forming in yolk sac and liver. Hepatic lobes, kidneys forming.
Wk 9-12: Face well formed. Head ½ of fetal size. Internal sex organs specific. Fingers /toes have nails. Amniotic fluid ~ 30 ml. Intestines undergo peristalsis, capable of absorbing glucose

Normal Fetal Development

Wk 13-16: liver and pancreas produce secretions. Muscles and bones developing
Wk 16: Myelination. Heart muscle well developed. Length 14-17 cm, 100 gm. + Hgb F/ Hgb A.
Wk 20: 300 gm. Sternum ossifies
Wk 24: 600 gm. Some fat depositing under wrinkled skin. Survival if born, rare.
Wk 25-28: Rapid brain development

Normal Fetal Development

Wk 28: 1050 gm. 37 cm. Surfactant low.
Accumulates most of iron and calcium in T3 when skeletal growth maximum and teeth forming
Wk 32: 1700 gm. 42 cm. If born, 90% survive
Wk 36: 2500 gm. 47 cm. Skin loses wrinkled appearance
Wk 40: 3200-3500 gm. 50 cm. HC 9.5 cm.

Pernoll. Current Obstetric and Gynecologic Diagnosis and Treatment. 7th ed. 1991
Worthington-Roberts and Williams. Nutrition in pregnancy and lactation 6th ed. 1997

Sites of Nutrient Absorption

Stomach: alcohol
Duodenum: Cl, S04, PO4, Fe⁺⁺, Ca⁺⁺, Mg⁺⁺, Zn⁺⁺.
Iodine throughout the gut
Jejunum: glucose, galactose, fructose, Vitamins C, B1, B2, B6, amino acids
Ileum: folate, Vitamins A D E K, Vitamin B12, fat, cholesterol
Colon: Sodium, potassium, Vitamin K (? Amt formed by bacterial action), Water

Krause 12th ed. 2008 page 19

Brain

[Adult] brain dependent on glucose & oxygen

Brain = 2% BW uses 15% daily energy ⁽¹⁾

28 weeker brain = 18% body weight ⁽²⁾

Term baby's brain = 10.5% body weight ⁽²⁾

Brain also with many nutrients

1. Guyton & Hall. 1996 2. Sinclair 1974 IN: Nutr in Development. 3. Steve Ringer 12/8/08 Personal communication

Folate

Functions:

Findings:

Vitamin K

Functions:

Findings:

Vitamin A

Functions:

Findings:

Vitamin D

Functions:

Findings:

Iodine

Functions:

Findings:

Iron

Functions:

Findings:

Weight ↓ and fat..

Organo-chloride pesticides and polychlorinated biphenyls (PCB's) **stored in adipose tissues**. SVOC's. (semi volatile organic compounds.) NHATS.

- ↑ pp DDT and PCB's (NE)
- ↑ Heptachlor epoxide (South)
- ↑ Hexachlorobenzene and pp DDE (West)

Wt ↓ in pregnancy → ↑ burn fat. Probable release of SVOC from adipose tissue.

Lordo et al. 1996

Back to the HG off-spring..

1. Brain development can be affected by lack of protein, carbohydrate and fats
2. Many nutrients can be implicated in cognitive dysfunction and poor anatomical development
3. Role of by-products of fat metabolism due to weight loss unexplored
4. At what level deprivation and duration produces a problem is unknown

Observations

1. Fetal development is complicated & clearly multi-factorial
2. Literature and studies suggest nutrition plays a significant role
3. Problems originating in gestation not always captured by immediate providers
4. What phrase would describe poor nutrition in pregnancy?
Fetal Origins of Adult Disease?
Maternal Origins of Fetal/Adult disease?
Developmental Origins of health and disease? (1) Prater 2008
Gestational Malnutrition?
5. How do we ensure developing fetus' obtains adequate nutrition to optimize future potential ?

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Gestational Malnutrition

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