Pregnancy and Long-Term Outcomes

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Family History



Pregnancy



Future Health

Hypothesis

Pregnancy complications identify families (women and children) at increased risk for long-term adverse health outcomes.

Lecture Outline

- Background
- Maternal Complications:
 - Gestational Diabetes
 - Preeclampsia
 - Others
- Barker Hypothesis

Physiologic Changes in Pregnancy

- Cardiovascular:
 - 30-50% increase in cardiac output, blood volume, and renal blood flow
 - 20-30 fold increase in uterine blood flow

- Endocrine:
 - 50-80% increase in insulin resistance

Decreased cellular immunity





Feig et al. CMAJ 2008;179:229-34

Consequences of GDM

- Maternal:
 - Type 2 Diabetes

• 5 years \rightarrow RR = 4.79; 10 years \rightarrow RR = 9.34

- Metabolic Syndrome
 - 20 years → RR 7.0
 - Further increase (2.4x) if >1 GDM pregnancy

Child

- Abnormal Glucose Metabolism
- Obesity
- Metabolic Syndrome

How to Follow Women with GDM?

- Follow-Up:
 - -ACOG, ADA, WHO -75 gm 2-hour OGTT.
 - -42 67% of US women with GDM have no follow-up glucose testing.
- What will increase follow-up rates in your practice?
- Breastfeeding:

>12 months of breastfeeding reduces T2DM risk by 14 – 27%.

Deaths from Heart Disease, USA



Heart Disease Mortality in Women and Men in Absolute Numbers, 1979 – 2004 (American Heart Association, 2007)

US Life Expectancy at Birth - Women





Irgens et al. BMJ 2001;323:1213-7

Cause-Specific Mortality Following Hypertensive Diseases of Pregnancy – Utah, 1939-2012*

- 60,580 women with <a>1 HDP in UPDB

 2 controls (age, year of birth, parity)
- All-cause mortality HR = 1.65 (95% CI 1.57-1.73)
- Greatest excess mortality risks:
 - Ischemic heart disease; HR = 2.23 (95% CI 1.90-2.63)
 - Diabetes; HR = 2.80 (95% Cl 2.20 3.55)
 - Stroke; HR = 1.88 (95% CI 1.53 2.32)
 - Alzheimer's Disease; HR = 3.44 (95% Cl 1.00 11.82)

*Thielen et al; 2016 Society for Maternal-Fetal Medicine



LEADING CAUSES OF DEATH BY AGE GROUPS - WOMEN AGES 35-64 - 2006

AGE	35-44	45-54	55-64
$N \longrightarrow$	30,893	69,859	112,414
RANK ↓			
1	Cancer – 25.7%	Cancer – 35.8%	Cancer – 41.0%
2	Injuries – 16.5%	Heart Disease – 15.3%	Heart Disease – 18.1%
3	Heart Disease – 12.0%	Injuries – 8.4%	COPD – 5.3%
4	Suicide – 4.9%	Stroke – 4.1%	Diabetes – 4.2%
5	HIV – 3.8%	Liver Disease – 3.1%	Stroke – 4.1%
6	Stroke – 3.4%	Diabetes – 3.1%	Injuries – 3.2%
7	Liver Disease – 2.9%	COPD – 2.8%	Liver Disease – 1.9%
8	Diabetes – 2.3%	Suicide – 2.6%	Kidney Disease – 1.7%
9	Homicide – 2.4%	HIV – 1.6%	Septicemia – 1.7%
10	COPD - 1.4%	Septicemia – 1.5%	Influenza/pneumonia – 1.1%

How do these statistics correlate with obstetric complications?

PRIMIGRAVID WOMEN EXPERIENCING PREGNANCY COMPLICATIONS AND THE RISK OF SUBSEQUENT DEATH FROM ANY CAUSE

PREGNANCY	ALL	WOMEN WITH	RATE/10,0	HR	95% CI	P-VALUE
OUTCOME	WOMEN	COMPLICATION	00			
			WOMAN-			
			YEARS			
Preterm	41,659	675	11.7	1.66	1.53,	<0.001
Delivery	(5.3%)	(1.6%)			1.79	
SGA	43,109	1,002	14.2	1.91	1.79,	<0.001
	(5.5%)	(2.3%)			2.04	
Gestational	7,449	115	10.3	1.23	1.03,	
Hypertension	(1.0%)	(1.5%)			1.48	
Mild pre-	26,810	364	8.7	1.11	1.00,	0.001
eclampsia	(3.4%)	(1.4%)			1.23	
Severe pre-	7,016	84	9.2	1.38	1.11,	
eclampsia	(0.9%)	(1.9%)			1.71	
Abruption	7,684	147	11.4	1.41	1.20,	<0.001
	(1.0%)	(1.9%)			1.67	
Stillbirth	4,039	98	15.6	1.83	1.50,	<0.001
	(0.5%)	(2.4%)			2.23	

Lykke JA et al. Paediatr Perinatal Epidemiol 2010;24:323-30.

PRIMIGRAVID WOMEN EXPERIENCING PREGNANCY COMPLICATIONS AND THE RISK OF SUBSEQUENT DEATH FROM NON-CARDIOVASCULAR CAUSES

PREGNANCY	ALL	WOMEN WITH	RATE/10,0	HR	95% CI	P-VALUE
OUTCOME	WOMEN	COMPLICATION	00			
			WOMAN-			
			YEARS			
Preterm	41,659	398	6.9	1.48	1.34,	<0.001
Delivery	(5.3%)	(1.0%)			1.64	
SGA	43,109	578	8.2	1.66	1.53,	<0.001
	(5.5%)	(1.3%)			1.82	
Gestational	7,449	50	4.5	0.82	0.62,	0.11
Hypertension	(1.0%)	(0.7%)			1.08	
Mild pre-	26,810	187	4.4	0.86	0.74,	
eclampsia	(3.4%)	(0.7%)			1.00	
Severe pre-	7,016	41	4.5	1.00	0.76,	
eclampsia	(0.9%)	(0.6%)			1.36	
Abruption	7,684	105	8.1	1.56	1.29,	<0.001
	(1.0%)	(1.4%)			1.89	
Stillbirth	4,039	62	9.9	1.79	1.39,	<0.001
	(0.5%)	(1.5%)			2.30	

Lykke JA et al. Paediatr Perinatal Epidemiol 2010;24:323-30.

What About Nulliparity?

- Nulliparity is consistently associated with an increased risk of ovarian cancer, including in BRCA1 and BRCA2 carriers¹.
- Same observation for endometrial and breast cancer².
- Mixed results for colon and rectal cancer³.

¹Modan et al. N Engl J Med 2001;345:235-40.
²Narold SA. Nat Rev Cancer 2002;2:113-33.
³Wernli et al. J Women's Health. 2009;18:995-1001.

Pregnancy and Subsequent Breast Cancer

- Long-recognized associations:
 - Reduced risk with young age of first birth
 - Reduced risk with increasing parity
- Most studies demonstrate decreased risks of breast and ovarian cancer in women with a history of preeclampsia (and their daughters).

Gender Differences in Mental Illness

More common in women (all > 2x):

- -Eating disorders,
- major depressive disorders,
- obsessive compulsive disorder,
- posttraumatic stress disorders,
- anxiety and panic disorders,
- seasonal affective disorder,
- Alzheimer's disease / dementia.

More common in men:

- Autism
- Schizophrenia.

Prevalence

- > 500,000 pregnancies / year (1 of every 8) complicated by psychiatric disorders (US).
- 13% of all psychiatric hospital admissions for women occur during the first postpartum year.
- Less than 20% of women who meet criteria for major depressive disorder seek treatment during pregnancy and the puerperium.

Graves' Disease

- 10x more common in women.
- 30% of women who are diagnosed with Grave's disease have been pregnant within the preceding 12 months.







David Barker (1938 – 2013)

Death rates from coronary heart disease among 15,726 men and women



birthweight (lbs)

Mean systolic pressure in men and women aged 60 - 71 years



birthweight (lbs)

Prevalence of insulin resistance syndrome in men aged 59 - 70



birthweight (lbs)

Conclusions - Mother

- Gestational Diabetes increases a woman's risk for T2DM. This risk can be reduced with:
 - Lifestyle modifications (diet, exercise, weight loss)
 Breastfeeding
- Preeclampsia increases a woman's risk for subsequent vascular disease and may reduce her risk for cancer.

Conclusions - Baby

- The best strategy to avoid the negative effects of fetal programming is to improve the health of young women via:
 - Better nutrition
 - Reduced stress
 - More exercise

 The health of the baby depends on the health of the mother before and after conception.

Comments? Questions?

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