

# The study in the relationship between intrauterine nutrition and carotid intimal media thickness in young adults.

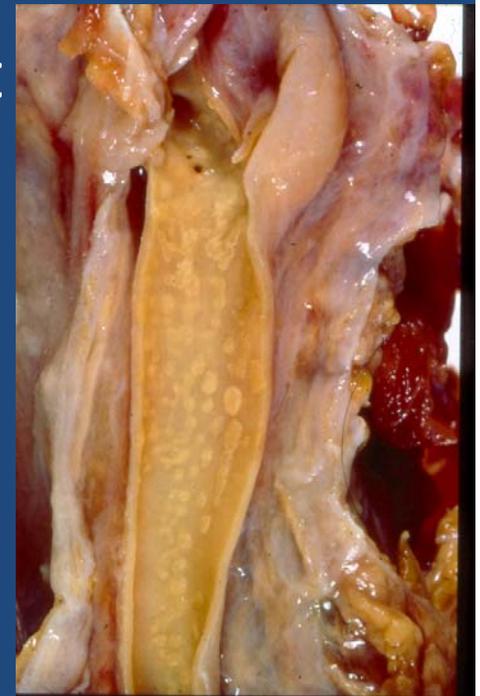


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# Topic

- Atherosclerosis
  - Progressive disease beginning early life<sup>1</sup>
  - Fatty streak, intimal thickening found in coronary, aorta same place with advanced lesion in adult<sup>2</sup>
  - Suggest a role of prenatal environment in atherogenesis

1. Stary HC. Atherosclerosis 1987;64:91-108.
2. Napoli C. J Clin Invest.1997;100:2680-2690.



# Animal study

- Rats exposed to energy and protein restricted diet



↑ endothelial dysfunction, HT of offsprings<sup>1</sup>

- Sheep exposed to energy restricted diet



↑ vascular dysfunction of adult offsprings<sup>2</sup>

1. Brawley L. Pediatr Res 2003;54:83-90

2. Torrens C. Exp Physiol 2009;94:1024-1033

# Research question

- Is there any relation in human between in characteristics of maternal diet during pregnancy and atherogenesis?
- Gale et al study in 216 nine year old children in UK\*  
Energy intake of mothers

↑ carotid intimal media thickness (CIMT)  
↓

Only one study in human maternal diet (in detail: protein, fat) and CIMT in 9 years old children

\* Gale Arterioscler Thromb Vasc Biol 2006;26:1877-82

# CIMT



- B mode ultrasound measurement of CIMT
  - Marker of early atherosclerosis<sup>1</sup>
  - Predict vascular event<sup>1</sup>
- CIMT role in children?
  - Many studies found children with hypercholesterolemia, obesity and high CIMT<sup>2</sup>
  - Exposure during childhood to cardiovascular risk factors predict CIMT in adult<sup>3</sup>

1) Lorenz. Stroke 2006;37:87-92. 2) Jarvisalo. Diabetes 2002;51:493-8 3) Raitakari JAMA 2003;290:2277-2283.

# Hypothesis

- If this relation “maternal diet-increased CIMT” is true, this should persist in older people (> 9 years) ?
- Is it true in Asian population?

# Method- 1990 study

- A study in Chiang Mai to identify the maternal risk factors of low birth weight(LBW) was conducted due to high rate of LBW in Chiang Mai(12%)
- This recruited 2184 pregnant women with gestational age (GA) < 24 weeks . Researcher s follow up every antenatal care up to delivery.
- Exclusion criteria : mothers who did not give birth in our centers, twins, stillbirth, abortion
- This study was approved by Local Ethic Committee and funded by Ford Foundation.

ราว 1990 ชื่อ-ชื่อ  
 ครอบคลุมไทยทั้งหมด



ราว 1990 มีอ-ชอ  
ครอบครัวไทยใหม่



# รศ.นพ.เพียร เชี่ยววานิช, PI 1990 study



# Maternal Risk factors

- Demographic data: age, underlying disease, level of education
- Antropometric data: height, weight, tricep skin fold, midarm circumference
- Socioeconomic data: saving, debt of wife and husband
- Complication during pregnancy and delivery
- Neonatal data: weight, height, chest-head circumference, placental data (diameter, cord length)
- Food diary: amount of energy, prot, fat and CHO in each 3 trimester was assessed. Nutritional information was collected by 2 methods. the 24-hour food recall method and the food frequency method.

# Method 1

- the 24-hour food recall method. Each subject was interviewed three times: WK 10 – 12: 1st trimester, WK 22 -24: 2<sup>nd</sup> trimester, WK 32 – 34: 3<sup>rd</sup> trimester
- The interview time for both questionnaire forms was about 15 minutes per subject.

(Cameron & Vanstaveren, 1988)

- Each respondent was asked to recall all food consumed during the previous day and to estimate quantities in ordinary measures or servings
- Using Thai Food Tables (Nutrition division, 1987 & 1992; RIHES\*), overall intakes at the three trimesters were calculated as energy, protein, fat and carbohydrate.

\*Division, Department of Health, Nutritional values of Thai food. 1<sup>st</sup> ed Veterans Organisation, 1992.

Nutritional Division, Department of Health, Nutritional values of Thai food. 4<sup>th</sup> ed, Nutritional Division 1987.

RIHES Unpublished document. Food composition table of Nutritive value of Northern Thai Food.

## Method 2

- The aim of the food frequency questionnaire approach is to assess average long term diet, for example, over weeks, months, or years, and is conceptually more related to average exposure than to intake on a few specific days.

## Our current study 2010

- Refresh address through many sources, wrote a letter(s) to all mothers who still lived in Chiang Mai and invited both mothers and offspings(in study 1990) to participate in our 2010 study. Adolescents age around 20 years old
- Of 2184, 564 mothers (26%) agreed to attend clinic. The invited people did not differ significantly in the mean birthweight and highest education in 1990.

	Participants	Outside study	Statistics (df)	P-value
	(N=564)	(N=1620)		
<b>Birth Weight(gms)</b>				
Mean $\pm$ SD	2974.98 $\pm$ 426.18	3011.34 $\pm$ 444.24	t (2182)=1.69	0.09
<b>Education of Mother</b>				
Never	3 (0.62%)	7 (0.53%)	$\chi^2(4) = 5.39$	0.25
Pratom	390(80.58%)	1020(77.16%)		
Mattayom	67(13.84%)	191(14.45%)		
Diploma $\geq$ BSc.	22(4.55%)	89(6.73%)		
Other	2(0.41%)	15(1.13%)		

# Method

- Offspring: (history of socioeconomic, education and underlying disease was also collected )
  - fasting blood sugar , 2 hours blood sugar after taking 75 gm of glucose
  - Fasting triglyceride, high density lipoprotein (HDL), cholesterol
  - Waist circumference
  - BP rest
  - HOMA
  - CIMT

# CIMT

- Investigator (KR) measured IMT at distal right common IMT using an Philip machine iE33 and a L10-4 MHz linear array transducer, while adolescents were recumbent.
- 6 longitudinal views including antero-posterior, lateral, antero-oblique were frozen at the end of diastolic phase. IMT of far wall was measured approximate 10 mm proximal to the beginning of the bifurcation using Q-Lab Philip software. The mean of 6 measurement of IMT were used in the analysis

# Analysis

- ANOVA, T test or Chi-Squared test to exam characteristics of participants
- Pearson correlation coefficients test the relations between characteristics and CIMT
- Linear regression calculate mean difference in CIMT according to trimester of nutrient intake
- Trend test look calculate the mean difference in CIMT when split data into 4 percentile group
- Local Research Ethics Committee approved the study and participants gave written consent.

# Result

- There are 564 offspring, mean age was 20 years. There were 30 participants with metabolic syndrome (6.1%)\* and 42 participants with small for gestational age(SGA)(8.5%).\*\*

\* Alberti Circulation 120.16 (2009): 1640-45.

\*\* SGA defined as < 10<sup>th</sup> percentile for each gestational age

# Features of participants at birth/20 yrs

	At birth	20 years
Female (%)	305 (54%)	-
Mean weight (Kg)	2.98 (2.94-3.01)	57.50 (56.30-58.69)
Mean BMI (Kg/m <sup>2</sup> )	-	21.30 (20.93-21.67)
Mean Ps (mmHg)	-	114.68 (113.61-115.76)
Mean Pd (mmHg)	-	73.44 (72.54-74.34)
Mean Cholesterol (mg/dL)	-	169.91 (166.82-172.99)
Mean Glucose (mg/dL)	-	82.77 (81.92-83.61)

BMI=body mass index, Ps=systolic blood pressure,  
Pd=diastolic blood pressure

## Correlation mother character during pregnancy with CIMT adjusted by offspring sex, smoking

Item	Pearson correlation	P value
Age at recruitment	- 0.04	0.35
Gestational age at first attending study	0.06	0.15
Gestational age at deliver	-0.01	0.98
Body mass index	-0.04	0.30
Parity	0.02	0.63

## Correlation of offspring character-CIMT adjusted by sex, smoke

Item	Pearson correlation	P value
Birth weight	0.06	0.17
Education	0.01	0.98
Body mass index	0.17	<0.01
Cholesterol	0.03	0.55
Fasting glucose	0.09	0.04
Systolic BP	0.12	0.02
Diastolic BP	0.04	0.36

## Correlation of offspring character-CIMT adjusted by sex, smoke

Item	Pearson correlation	P value
Birth weight	0.06	0.17
Education	0.01	0.98
Body mass index (Weight)	0.17	<0.01
Cholesterol	0.03	0.55
Fasting glucose	0.09	0.04
Systolic BP	0.12	0.02
Diastolic BP	0.04	0.36

# Characteristics of maternal diet of participants at 1<sup>st</sup> and 3<sup>rd</sup> trimester

Item	1 <sup>st</sup> trimester		3 <sup>rd</sup> trimester	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Weight gain	-0.12	0.35	0.03	0.95
Protein intake	-0.19	0.03	0.07	0.12
Fat intake	-0.21	0.02	0.05	0.29
Carbohydrate intake	-0.03	0.77	0.08	0.11
Energy intake	-0.11	0.23	0.09	0.05

*r*=correlation coefficients, *P* = *P* value

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*r*=correlation coefficients, *P* = *P* value

## Difference of CIMT, adjusted for child characteristics- sex, smoking, BMI, plasma glucose, systolic BP

Maternal nutrient intake	Mean difference of CIMT (95% Confidence interval)
Protein intake	
1 (Percentile 1-25)	0.4447 (0.4363-0.4531)
2 (Percentile 26-50)	0.4409 (0.4355-0.4462)
3 (Percentile 51-75)	0.4370 (0.4316-0.4424)
4 (Percentile 76-100)	0.4331 (0.4248-0.4415)
<i>P</i> for trend	<b>0.035</b>
Fat intake	
1 (Percentile 1-25)	0.4450 (0.4364-0.4535)
2 (Percentile 26-50)	0.4410 (0.4355-0.4465)
3 (Percentile 51-75)	0.4370 (0.4317-0.4424)
4 (Percentile 76-100)	0.4331 (0.4247-0.4414)
<i>P</i> for trend	<b>0.034</b>

# Discussion

- CIMT is thicker in adolescent whose mothers had a lower protein/fat intake during pregnancy



provide evidence

Maternal diet in pregnancy might influence the susceptibility to atherogenesis of offsprings

# Supporting studies

- Many animal studies: restricted maternal diet in rat → impaired endothelial function
- Epidemiological studies
  - Dutch Hunger Winter, Pregnancy during Famine in Western part of Netherlands 1<sup>st</sup> trimester cause dyslipidemia in offsprings<sup>1</sup>
  - Parker hypothesis: SGA associated with stroke, CAD in adult<sup>2</sup>

<sup>1</sup> Roseboom. Am J Clin Nutr 2000;72:1101-6

<sup>2</sup> Martyn Lancet 1996;348:1264-8.

# Mechanism

- Partly Associated with
  - higher BMI (heavier at 20 yrs)
  - Higher fasting blood glucose
  - Higher systolic blood pressure

Add early exposure to cardiovascular risk factors  
may promote atherogenesis

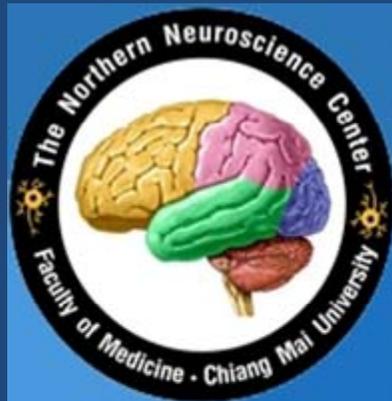
# Limitation

- We can follow up 29% of the 1990 cohort
- No data breast feeding
- Recall food diary

# Conclusion

- Lower protein/fat intake during pregnancy may increase susceptibility to atherogenesis of offsprings

# Thanks to all funding bodies



ศูนย์โรคสมองภาคเหนือ

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Thank you