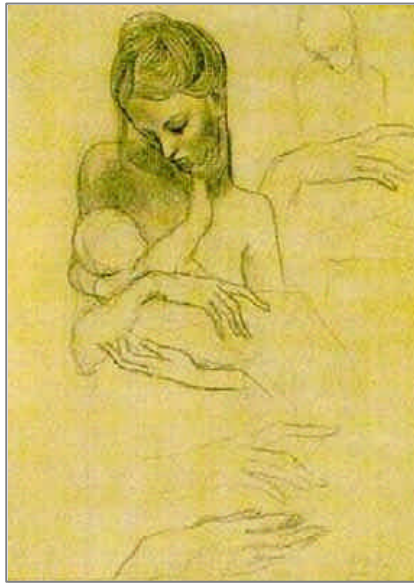


Nutritional Influences in Pregnancy and Postpartum for Women and their Children



Pablo Picasso - Mother and child
and four sketches of the right hand

Alexis J Hure, BND (Hons I)

A thesis submitted to the University of Newcastle,
Australia in fulfilment of the requirements of the
degree of Doctor of Philosophy (PhD)

December 2008

Statement of Originality

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent to this copy of my thesis, when deposited in the University Library**, being made available for loan and photocopying subject to the provisions of the Copyright Act 1968.

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Declaration of Collaboration

The work embodied in Chapter 4 (Diet and Pregnancy Status in Australian Women) has been published in Public Health Nutrition, an international peer-reviewed journal.

This work was completed in collaboration with Dr Anne Young from Women's Health Australia. Dr Anne Young performed the statistical analyses for this paper and provided intellectual input for the development of the manuscript.

Associate Professor Clare Collins (primary PhD supervisor) and I attest to the significant and independent contribution I have made to this paper. This has been formally recognised with leading authorship on this publication.

All other work contained within this thesis was completed with appropriate input and guidance from my PhD supervisors, Associate Professor Clare Collins and Professor Roger Smith.

.....

Clare E Collins

.....

Alexis J Hure

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List of Abbreviations

ABCD Obesity	Assessment Before Children Develop Obesity
AC	Abdominal circumference
ACCVFFQ	Anti Cancer Council of Victoria Food Frequency Questionnaire
AGA	Appropriate for gestational age
AI	Adequate intake
ALSPAC	Avon Longitudinal Study of Parents and Children
ALSWH	Australian Longitudinal Study on Women's Health
ANOVA	Analysis of variance
ARFS	Australian Recommended Food Score
BMI	Body mass index
BMR	Basal metabolic rate
BPD	Biparietal diameter
CE	Coefficient
CHD	Coronary heart disease
CI	Confidence interval
CSIRO	Commonwealth Scientific and Industrial Research Organisation
DEXA	Dual energy x-ray absorptiometry
DNA	Deoxyribonucleic acid
DOHaD	Developmental origins of health and disease
DQES	Dietary Questionnaire for Epidemiological Studies
DQI-P	Diet Quality Index for Pregnancy
EAR	Estimated average requirement
FFQ	Food frequency questionnaire
FL	Femur length
FOAD	Fetal Origins of Adult Disease
Folbp1	Folate-binding protein one
HAPS	Hunter Area Pathology Service
HC	Head circumference
HDL-C	High density lipoprotein-cholesterol
HHS	Hordaland Homocysteine Study
holoTC	holotranscobalamin
IF	Intrinsic factor
ISAK	International Society for the Advancement of Kinanthropometry
IUGR	Intrauterine growth restriction
kcal	Kilocalorie
kg	Kilograms
LBW	Low birthweight
LDL-C	Low density lipoprotein-cholesterol
LMP	Last menstrual period
Math Model	Mathematical Model of Pregnancy
MJ	Megajoule

MMA	Methylmalonic acid
MMA-CoA	Methylmalonyl coenzyme A
MRI	Magnetic resonance imaging
mTHF	Methyltetrahydrofolate
NATA	National Association of Testing Authorities
NHMRC	National Health and Medical Research Council
NRVs	Nutrient Reference Values
NSW	New South Wales
NTDs	Neural tube defects
NUTTAB	Nutrient tables for use in Australia
OR	Odds ratio
PAR	Predictive adaptive response
pB12	Plasma vitamin B12
pHcy	Plasma homocysteine
PhD	Doctor of Philosophy
PPAQ	Pregnancy Physical Activity Questionnaire
PPAR-α	Peroxisome proliferator-activated receptor- α
PTD	Preterm delivery
rcFol	Red cell folate
RDI	Recommended dietary intake
RNA	Ribonucleic acid
RR	Relative risk
SAS	Statistical Analysis Systems
SD	Standard deviation
SE	Standard error of the mean
SGA	Small for gestational age
SIDS	Sudden infant death syndrome
Suc-CoA	Succinyl-CoA
TC	Transcobalamin
THF	Tetrahydrofolate
TIHS	Tasmanian Infant Health Survey
TNF-α	Tumour necrosis factor- α
UK	United Kingdom
UL	Upper level
USA	United States of America
WATCH	Women and their Children's Health
WFR	Weighed food record
WHO	World Health Organization

Thesis Publications and Presentations

AWARDS

- 1) Nutrition Society of Australia, Early Career International Conference Scholarship, awarded December 1, 2008.
- 2) The University of Newcastle, Faculty of Health, 10 of the Best, Research Higher Degrees Showcase Finalist, awarded September 26, 2008.

PUBLISHED ARTICLES

- 1) Hure A, Young A, Smith R, Collins C. Diet and pregnancy status in Australian women. *Public Health Nutrition* 2008; 1-9.
- 2) Hure AJ, Smith R, Collins CE. A recruiting failure turned success. *BMC Health Services Research* 2008; 8:64.

ORAL PRESENTATIONS WITH PUBLISHED ABSTRACTS

- 1) Hure AJ, Collins CE, Smith R. Maternal and infant vitamin B12, folate and homocysteine in pregnancy and postpartum. Proceedings of the Nutrition Society of Australia 32nd Annual Scientific Meeting, *Asia Pacific Journal of Clinical Nutrition* 2008; 17 (Suppl 3): S96.
- 2) Hure AJ, Giles WB, Smith R, Collins CE. Maternal weight change in pregnancy predicts fetal size but not adiposity. Proceedings of the 4th Australian Health and Medical Research Congress 2008: p.284.
- 3) Hure AJ, Young AF, Smith R, Collins CE. Is diet quality higher during pregnancy? Proceedings of the Perinatal Society of Australia and New Zealand 11th Annual Congress, *Journal of Paediatrics and Child Health* 2007; 43 (Suppl 1): A43-44.

- 4) Hure AJ, Young AF, Smith R, Collins CE. A comparison of diet quality in young Australian women according to pregnancy status. Proceedings of the Nutrition Society of Australia 30th Annual Scientific Meeting, Asia Pacific Journal of Clinical Nutrition 2006; 15 (Suppl 3): S53.

POSTER PRESENTATIONS WITH PUBLISHED ABSTRACTS

- 1) Hure A, Wright I, Smith R, Collins C. Nutrient supplementation in pregnancy: development of evidence-based best-practice guidelines. Proceedings of the Perinatal Society of Australia and New Zealand 13th Annual Congress, Journal of Paediatrics and Child Health 2009; 4(Suppl.1): A124.
- 2) Hure AJ, Collins CE, Smith R. Maternal weight change in pregnancy predicts fetal size but not adiposity. Proceedings of the 56th Annual Meeting of the Society for Gynecologic Investigation, Reproductive Sciences 2009;16(3): 555.
- 3) Hure AJ, Collins CE, Smith R. Maternal pregnancy folate predicts homocysteine in the six month old infant. Proceedings of the 56th Annual Meeting of the Society for Gynecologic Investigation, Reproductive Sciences 2009;16(3): 556.
- 4) Hure AJ, Smith R, Giles W, Somerset D, Collins CE. Fetal fatness is not associated with maternal adiposity in pregnancy. Proceedings of the 5th International Congress on the Developmental Origins of Health and Disease, Early Human Development 2007; 83 (Suppl 1): S161.
- 5) Hure AJ, Smith R, Collins CE. Methodological barriers to studying the predictive adaptive response in humans. Proceedings of the 10th International Congress on Obesity, Obesity Reviews 2006; 7 (Suppl 2): 152.
- 6) Hure AJ, Smith R, Collins CE. Energy intake versus expenditure in breastfed infants: Aren't we missing something? Proceedings of the Dietitians Association of Australia 24th National Conference, Nutrition and Dietetics 2006; 63 (Suppl 1): A40.

INVITED SPEAKER PRESENTATIONS

- 1) Hure AJ. A nutritional journey. Proceedings of the John Hunter Children's Hospital Annual Neonatal Seminar, Hunter Valley, Australia, April 11, 2008.
- 2) Hure AJ, Smith R, Collins CE. Nutritional genomics concerning mothers and babies. Meeting of the Newcastle Branch of the Nutrition Society of Australia, Newcastle, Australia, August 25, 2006.

Abstract

Maternal factors prior to conception and during pregnancy may influence the development of the metabolic, cardiovascular and endocrine systems of the offspring and subsequent disease pathogenesis. This thesis explores the concept of the developmental origins of health and disease.

Human observational research studies were undertaken to test the relationships amongst maternal dietary intake, weight gain during pregnancy and changes in biochemical markers between pregnancy and postpartum for the mother and infant. This thesis presents three chapters of original research related to maternal and fetal nutrition, and one chapter of empirical data concerning the methodological challenges faced when recruiting for research purposes.

An analysis of dietary intake data from the young cohort of the Australian Longitudinal Study on Women's Health was used to determine the overall diet quality in a contemporary cohort, and to assess whether those who are pregnant eat differently to those who are not. Only small differences in diet quality and nutrient intakes were detected between pregnancy groups, and diet quality scores were consistently low. When the intake data were compared to Australian recommendations it appears that many young women fail to reach key nutrient targets, including those set for folate, fibre, calcium, iron, potassium and vitamin E.

The research focus then shifted to prospective longitudinal data collection for women and their children during pregnancy and after birth. Low recruitment to this component of the studies threatened the potential to achieve the research aims. Rather than jeopardising the power of the investigations efforts were made to understand what had gone wrong and how the situation could be rectified.

An investigation of the relationship between fetal adiposity and maternal weight changes in pregnancy was performed. Pre-pregnancy body mass index (BMI) and weight changes during pregnancy were taken as broad markers of maternal nutritional status and energy regulation. Intrauterine growth, including the accumulation of adipose tissue, was assessed using serial ultrasounds. Fetal size was positively related to maternal pre-pregnancy weight (and BMI) and weight gain (change in BMI) during

pregnancy. Maternal pre-pregnancy weight was positively associated with adiposity at the fetal abdomen, but not the thigh. However, overall maternal weight gain was not associated with fetal adiposity.

To then determine whether maternal vitamin B12 and folate (methyl donors) in pregnancy could influence the offspring's homocysteine metabolism at birth, changes in plasma vitamin B12, plasma folate and red cell folate were characterised for the cohort of more than 100 women during pregnancy and up to six months after birth. A small sub-sample of infants also had blood collected at six months postpartum. Average maternal plasma folate during pregnancy was significantly predictive of infant plasma homocysteine.

In conclusion, the research outlined herein demonstrates important interactions between the mother and her offspring during the critical windows of early development. The research is multidisciplinary in its application and contributes to our understanding of some of the nutritional influences in pregnancy and postpartum for women and their children.