

THE INFLUENCE OF MODERATE AND HIGH FORMULA  
DOCOSAHEXAENOIC ACID ON TERM BABOON NEONATE TISSUE  
COMPOSITION AND CLINICAL PARAMETERS

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by

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Long-chain polyunsaturated fatty acids (LCPUFA) are indispensable for normal infant growth and development. Docosahexaenoic acid (DHA, 22:6n-3) and arachidonic acid (ARA, 20:4n-6) are LCPUFA that play a critical role in central nervous system development. During the brain growth spurt, rapid accumulation of LCPUFA occurs in the brain and retina. Currently, insufficient evidence exists to determine optimal levels of dietary LCPUFA required during the perinatal period.

In the context of a safety and efficacy study of dietary LCPUFA in baboon neonates, we examined the influence of medium and high levels of formula DHA levels on tissue fatty acid composition and hematological and clinical chemistry measures. Infant formulas were fed from birth to 12 weeks of age: Control (C, no DHA/ARA); 1× LCPUFA (L, 0.32%DHA/0.64%ARA); 3× LCPUFA (L3, 0.96%DHA/0.64%ARA).

At 12 weeks, tissue DHA levels were more sensitive to dietary manipulations than ARA. While DHA in the cerebral cortex increased with higher concentrations of DHA, no differences between L and L3 were detected in the basal ganglia and limbic system. These findings indicate that current levels of LCPUFA in infant formula are not sufficient to optimize DHA levels in the developing cortex.

RBC, hematocrit, hemoglobin, and red blood cell distribution width (RDW) were significantly elevated by formula DHA and ARA. All erythrocyte values were

within accepted normal ranges for infant baboons and no differences were detectable at 12 weeks. These data provide the first indication that dietary LCPUFA may influence hematopoiesis during the first weeks of life and mitigate the precipitous decline in red cell values associated with neonatal anemia.

All clinical chemistry parameters were normal up to 12 weeks of age. Many of the trends observed were similar to those documented in human infant development. No negative effects on growth measures, hematological or clinical assessments were observed between formula groups. These results suggest that levels of DHA higher than presently included in US infant formulas enhance cerebral cortex DHA and may provide additional benefits by improving erythropoiesis. They also provide a basis for interpretation of parallel human infant studies currently underway.

## BIOGRAPHICAL SKETCH

Andrea T. Hsieh was born on October 21, 1978 in Elmhurst, Illinois. She was the oldest of four children and spent her childhood and adolescent years in the sprawling suburbs of Chicago. She attended the University of Illinois Urbana-Champaign and received a Bachelors of Science in Biochemistry. In 2000, she moved to Ithaca, NY and joined the Division of Nutritional Sciences at Cornell University.

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## TABLE OF CONTENTS

### **CHAPTER 1. INTRODUCTION**

1.1 BACKGROUND	1
1.2 METABOLISM OF n-3 AND n-6 FATTY ACIDS	1
1.3 ESSENTIAL FATTY ACID DEFICIENCY	6
1.4 ESSENTIAL FATTY ACID CONVERSION TO LCPUFA	8
1.5 LCPUFA SYNTHESIS IN NEONATES	8
1.6 LCPUFA DURING THE PERINATAL PERIOD	9
1.7 NHP MODELS FOR HUMAN INFANT DEVELOPMENT AND FA METABOLISM	12
1.8 INFLUENCE OF LCPUFA ON INFANT NEURODEVELOPMENT AND GROWTH	13
1.9 LCPUFA IN HUMAN MILK AND INFANT FORMULA	18
1.10 SUMMARY	22
1.11 REFERENCES	23

### **CHAPTER 2. THE INFLUENCE OF MODERATE AND HIGH LEVELS OF LONG CHAIN POLYUNSATURATED FATTY ACID (LCPUFA) SUPPLEMENTATION ON BABOON NEONATE TISSUE FATTY ACIDS**

2.1 ABSTRACT	30
2.2 INTRODUCTION	31
2.3 MATERIALS AND METHODS	33
2.3.1 Animals	33
2.3.2 Diets	33
2.3.3 Growth	34
2.3.4. Sampling	34



2.3.5 Fatty Acid Analyses	36
2.3.6 Statistics	36
2.4 RESULTS	
2.4.1 Formula Consumption and Growth	37
2.4.2 RBC and Plasma Fatty Acids	37
2.4.3 Liver and Heart Fatty Acids	38
2.4.4 Retina Fatty Acids	38
2.4.5 Central Nervous System Fatty Acids	39
2.5 DISCUSSION	51
2.6 CONCLUSION	54
2.7 ACKNOWLEDGEMENTS	55
2.8 REFERENCES	56
<b>CHAPTER 3. FORMULA DOCOSAHEXAENOIC ACID AND</b>	
<b>ARACHIDONIC ACID IMPROVES POSTNATAL HEMOGLOBIN</b>	
<b>AND RELATED INDICES IN TERM BABOON NEONATES</b>	
3.1 ABSTRACT	59
3.2 INTRODUCTION	60
3.3 MATERIALS AND METHODS	
3.3.1 Animals and Diets	62
3.3.2 Blood Sampling	63
3.3.3 Hematology	63
3.3.4 Statistics	64
3.4 RESULTS AND DISCUSSION	64
3.5 CONCLUSION	74
3.6 ACKNOWLEDGEMENTS	75
3.7 REFERENCES	76

**CHAPTER 4. BIOCHEMICAL AND HEMATOLOGICAL PROFILES OF  
BABOON NEONATES CONSUMING FORMULAS WITH  
MODERATE AND HIGH DIETARY LONG-CHAIN  
POLYUNSATURATED FATTY ACIDS**

4.1 ABSTRACT	80
4.2 INTRODUCTION	81
4.3 MATERIALS AND METHODS	
4.3.1 Animals and Diets	82
4.3.2 Blood Sampling	83
4.3.3 Clinical Chemistry and Hematology	83
4.3.4 Statistics	84
4.4 RESULTS AND DISCUSSION	
4.4.1 Clinical Chemistry	85
4.4.2 White Cell Measurements	89
4.5 CONCLUSION	92
4.6 ACKNOWLEDGEMENTS	92
4.7 REFERENCES	93

**CHAPTER 5. CONCLUSION and FUTURE STUDIES**

5.1 SUMMARY	96
5.2 REFERENCES	98

## LIST OF FIGURES

1.1 Metabolic pathways for the conversion of linoleic acid and $\alpha$ -linolenic acid into LCPUFA.	3
1.2 Conversion of linoleic acid to arachidonic acid.	4
2.1 Summary of baboon neonate formula consumption and growth.	47
2.2 Baboon neonate FA concentrations at 12 weeks of age.	49
3.1 Regression analysis calculation for RBC, Hemoglobin, Hematocrit and RDW.	65
3.2 Regression analysis calculation for MCV, MCH and MCHC.	69
4.1 Clinical chemistry parameters influenced by dietary LCPUFA.	88

## LIST OF TABLES

1.1 Common dietary sources of n-6 and n-3 fatty acids.	3
1.2 Target LCPUFA concentrations in US commercial term infant formulas.	21
2.1 Characteristics of baboon neonate groups.	34
2.2 Nutrient content of Enfamil <sup>®</sup> LIPIL <sup>®</sup>	35
2.3 Liver, RBC, plasma and heart FA composition.	41
2.4 Cerebral cortex precentral gyrus and frontal lobes and retina FA composition.	43
2.5 Basal ganglia (globus pallidus, putamen, caudate) and amygdala FA composition.	44
2.6 Superior and inferior colliculi FA composition.	46
3.1 Characteristics of baboon neonate groups.	63
4.1 Characteristics of baboon neonate groups.	84
4.2 Changes in clinical chemistry parameters for baboon neonates at 6 and 12 weeks of age.	88
4.3 Ontogeny of white cell parameters for baboon neonates from 2 to 12 weeks of age.	90

## LIST OF ABBREVIATIONS

- ALA,  $\alpha$ -linolenic acid (18:3n-3)
- ARA, arachidonic acid (20:4n-6)
- C, Control formula: DHA (0%w/w), ARA (0%w/w)
- CBC, complete blood count
- CNS, central nervous system
- DHA, docosahexaenoic acid (22:6n-3)
- DHGLA, dihomo- $\gamma$ -linolenic acid (20:3n-6)
- DPA, docosapentaenoic acid (22:5n-3, 22:5n-6)
- EDTA, ethylenediaminetetraacetic acid
- EFA, essential fatty acid
- EPA, eicosapentaenoic acid (20:5n-3)
- EPO, erythropoietin
- ERG, electroretinography
- FA, fatty acid
- FAME, fatty acid methyl ester
- GC, gas chromatography
- GI, gastrointestinal tract
- GLA  $\gamma$ -linolenic acid (18:3n-6)
- IUGR, intrauterine growth restriction
- L, LCPUFA intermediate formula: DHA (0.32%), ARA (0.64%)
- L3, LCPUFA high formula: DHA (0.96%), ARA (0.64%)
- LA, linoleic acid (18:2n-6)
- LCPUFA, ( $\geq 20$  carbons) long-chain polyunsaturated fatty acids
- MCV, mean cell volume

MCH, mean cell hemoglobin  
MCHC, mean cell hemoglobin concentrations  
MDI, Mental Development Index  
MPV, mean platelet volumes  
MS, mass spectrometry  
MUFA, monounsaturated fatty acids  
NEC, necrotizing enterocolitis  
NHP, non-human primate  
PDI, Psychomotor Development Index  
RBC, red blood cells  
RDW, red blood cell distribution width  
SID, Bayley Scales of Infant Development  
SFA, saturated fatty acids  
VEP, visual evoked potential  
VLBW, very low-birth weight  
WBC, white blood cell  
w/w, weight ratio of FA to total FA