#### IMMUNOMODULATORY EFFECTS OF FOODS

Essay
Submitted for partial fulfillment of Master Degree
in Pediatrics

By
Islam Massoud Soliman
M. B. B. Ch. AlAzhar University
1999

Under supervision of

#### **Professor Yehia Mohamed El-Gamal**

Professor of Pediatrics, Founder of Pediatric Allergy and Immunology Unit Ain Shams University

#### Dr. Ola Abd Elaziz Elmasry

Assistant Professor of Pediatrics Faculty of Medicine Ain Shams University

Faculty of medicine
Ain Shams University
2010

تطوير المناعة بالغذاء مقالة توطئه للحصول على درجة الماجستير في طب الأطفال

مقدمة من الطبيب /إسلام مسعود سليمان بكالوريوس الطب والجراحة 1999 كلية الطب – جامعة الأزهر

تحت إشراف أ.د/ يحيى محمد الجمل أستاذ طب الأطفال مؤسس وحدة الحساسية والمناعة للأطفال كلية الطب – جامعة عين شمس

أ.م / علا عبد العزيز المصرى
 أستاذ مساعد طب الأطفال
 كلية الطب – جامعة عين شمس

كلية الطب – جامعة عين شمس **2010** 

#### **ACKNOWLEDGEMENT**

First and foremost, thanks and praise to Allah, most gracious, most merciful.

I wish to express my deepest appreciation and respect for Dr: Yehia Mohammed El-Gamal, Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for his valuable guidance, kind advice and useful help through out this work.

Also I wish to express my sincere thanks and deepest gratitude to Dr Ola Abd Elaziz Elmasry Assistant Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for her generous encouragement, and continuous supervision during this work.

## **Contents**

List of Abbreviation	onsi
List of Tables	v
List of Figures	vi
Copy of study p	rotocol
□ Introduction	& Aim of the Work1
□ Review of Lit	terature5
• Modulation	of Immune Functions by Foods5
- Foods	<b>Capable of Improving Immune Functions</b>
in Health	y Individuals7
	Capable of Improving Clinical Symptoms in
	With Hypersensitivity:9
- Foods	Capable of Improving Immune Functions in
Subjects	in an Immunocompromised State:11
• Mechanisms by	which Foods Influence Immune Functions13
- The Bas	10
	sic Nutrients:13
0	
0	Fatty Acids:
0	Fatty Acids:
0	Fatty Acids:
• • • <b>The Mi</b>	Fatty Acids:       .13         Amino Acids:       .18         Carbohydrates       .23         cronutrients:       .25         Vitamins:       .25         ○ Vitamin A:       .25         ○ Antioxidant Vitamins and Immune       .31         ■ Vit C       .32
• • • <b>The Mi</b>	Fatty Acids:
• • • <b>The Mi</b>	Fatty Acids:

	0	Minerals       .44         o Zinc       .44         o Iron       .49         o Selenium       .52
	0	Probiotics
•	Foods beneficial	to the immune system62
	-	Strawberries, etc62
	-	Apples <b>66</b>
	-	Carrots, Cellary and Parsley69
	-	Cruciferous vegetables72
	-	Tomatos
	-	Garlic
	-	Legumes82
	-	Cereals
	-	Nigella sativa (black seed)87
	-	Curcumin92
	-	Dairy products and cheese93
	-	Honeybee103
	-	Mushrooms105
	-	Caffeine and Tea107
	-	Common herbs110
	-	Ginseng112
	-	Olive oil and The Mediterranean Diet112
	-	Echinacea114
	• Foods har	rmful to the immune system117
	Summary and	Conclusions137
	Recommendat	ions142
	References	146
	Arabic Summ	nary1

## List of abbreviations

ABL	Agarius Bisporus Lectin
AE	Acrodermatitis Enteropathica
AIDS	Acquired Immune Deficiency
	Syndrome
ALRI	Acute Lower Respiratory Infection
APAL	Apalbumin
APAL-F1	Recombinant Apal Fragment-1
APC	Antigen Presenting Cells
APP	Auricularia Polytricha Protein
CAMP	Cyclic Adenosine Monophosphate
CAT-2	Catalase 2
CD	Cluster Of Differentiation
CLA	Conjugated Linoleic Acid
CON-A	Concanavalin A
COX	Cyclo-oxygenase
CRC	Colo Rectal Carcinoma
CRP	C- Reactive Protein
CTL	Cytotoxic T Lymphocyte
CVs	Cruciferous Vegetables
Da	Dalton
DBPCFC	Double- Blind Placebo – Controlled
	Food Challenge
DGLA	Dihomo-Gamma-Linolenic Acid
DHA	Docosahexaenoid Acid
DNA	Deoxy Ribonucleic Acid
DSS	Dextran Sulphate Sodium
DTH	Delayed Type Hypersensitivity
DTQ	Dithymaquinone

ECD	Desir aubil Cationia Dustain
ECP	Eosinophil Cationic Protein
EE	Eosinophilic Esophagitis
EGIDS	Eosinophilic Gastrointestinal Disorders
EPA	Eicosapentaenoic Acid
EPX	Eosinopil Protein X
FIEA	Fluorescent Enzyme Immuno-Assay
FPIES	Food Protein- Induced Enterocolitis
	Syndrome
GAIT	Gut Associated Lymphoid Tissue
GAPDH	Gamma Amino Puteric Dehydrogenase
GI	Gastro-intestinal
GIT	Gastro-intestinal Tract
GM-CSF	Granulocyte Macrophage Colony
	Stimulating Factor
GSH	Glutathione
GT	Glutathione Transferase
HETE	Hydroxy Eicosa Tetra Enoic Acid
HIF	Hypoxia Inducible Factor
HIV	Human Immunodeficiency Virus
HLA	Human Leukocytic Antigen
IBD	Inflammatory Bowel Disease
IEL	Intra Epithelial Lymphocytes
Ig	Immunoglobulin
IKBA	Inhibitor Of Kappa B Alpha
IKK	Inhibitor Of Kappa B Kinase
IL	Interleukin
INOS	Inducible Nitric Oxide Synthase
IP <sub>10</sub>	Interferon Gamma Inducible Protein Of
-	10 KD
ITAC	Inducible T-Cell A Chemoattractant

KD	Kilo Dalton
LA	Linoleic Acid
LAB	Lactic Acid Bacteria
LDH	Lactate Dehydrogenase
LOX	Lipo-Oxygenase
LPS	Lipopolysaccharide
LT	Leukotriens
MDP	Muramyl Dipeptide
MHC	Major Histocompitability Complex
MIG	Monokine Induced By INF-Gamma
NFKB	Nuclear Factor Kappa B
NK	Natural Killer
NO	Nitric Oxide
NS	Nigella Sativa
PBMC	Peripheral Blood Mononuclear Cells
PG	Prostaglandin
PHA	Phytohemagglutinin
PKA	Protein Kinase A
PMN	Peripheral Mononuclear Cells
RAE	Retinol Activity Equivalents
RASTS	Radio-allergo-sorbant Tests
RCT	Randomized Controlled Trial
RDA	Recommended Dietary Allowance
RE	Retinol Equivalent
RJ	Royal Jelly
RNA	Ribonucleic Acid
ROS	Reactive Oxygen Species
RPA	RNA Protection Assay
SCID	Severe Combined Immune Deficiency
SCORAD	Scoring of Atopic Dermatitis

SIgA	Secretory Immunoglobulin A
STZ	Streptozatocin
TGF	Transforming Growth Factor
Th	T helper
TLR	Toll – Like Receptor
TNFA	Tumor Necrosis Factor Alpha
TQ	Thymoquinine
TX	Thromboxane
UL	Upper Intake Level
UV	Ultra Violet
VCAM	Vascular Cell Adhesion Molecule
Zn	Zinc

## List of Tables

NO	Title	Page
1	Parameters available for evaluating the immune-	6
	modulating effects of foods in humans	
2	Dietary sources of antioxidant vitamins	32
3	Vitamin C content of citrus fruits and juices	33
4	Carotenoid and vitamin A contents of citrus	36
	fruits and juices	
5	Folate content of citrus fruits and juices	40
6	Vitamin B6 content of citrus fruits and juices	42
7	Dietary Reference Intake (DRI) of some	43
	vitamins recommended for infants and children	
8	The 95 percent predictive IgE levels for the most	122
	common foods.	
9	Natural history of food allergy and cross	133
	reactivity between common food allergies	

# List of Figures

NO	Title	Page
1	Modulation of immune function by foods	8
2	Outline of synthesis of eicosanoids from 20-	17
	carbon n-6and n-3 polysaturated fatty acids	
3	Regulation of Th1/Th2 interaction by iron	51
	through inhibiting IFNy activity	
4	Strawberry	62
5	Pepper plant	63
6	Blossoms, fruits, and leaves of the apple tree	66
	(Malus domestica)	
7	Harvested carrots	69
8	Parsley	70
9	Cabbage	72
10	Cauliflower	72
11	Broccoli	73
12	Tomato	74
13	Allium sativum, known as garlic	76
14	Soybean	82
15	Wheet	84
16	Nigella Sativa	87
17	Honey comb	103
18	(Agaricus bisporus), one of the most widely	105
	cultivated mushrooms in the world.	
19	Echinacea	114
20	Evaluation of IgE mediated gastrointestinal	134
	disorders	
21	Evaluation of non IgE mediated	135
	gastrointestinal disorders	
22	Evaluation of mixed immune - mediated	136
	gastrointestinal disorders. Eosinophilic	
	esophagitis	

#### INTRODUCTION

Many fundamental principles in nutritional immunology have emerged over the years and provide the basis for analysis of antioxidant nutrition and immunity. These include the following:

- 1. Nutrition can affect innate immunity such as barriers to infection, mucosal surfaces, complement, natural killer (NK) and polymorphonuclear cell functions.
- 2. Nutrients can also effect a decrease or increase and therefore imbalance, in the ratio of T- to B-cells, their subsets, e.g., CD4<sup>+</sup> to CD8<sup>+</sup> ratio, lymphoproliferation, cytokine balance, and antibody production and function.
- 3. Lymphoid tissues and cells are particularly vulnerable to environmental (e.g., nutritional) insult during fetal and neonatal growth and differentiation (vulnerable period), which can have short-term- as well as long-term-consequences.
- 4. Pathological nutritional deficits can impact the immune response in both developed and developing countries. For example, infection can induce similar immunological changes to that observed under different nutritional states, and can induce metabolic effects on nutritional status, e.g., the

effect of measles on vitamin A, Epstein-Barr virus infection (and HIV) on essential fatty acid status.

5. The nutrition-immunity-infection model has been classically considered a more-or-less "one way" model, but there is also evidence for reverse flow, that is, nutrients can affect genotype and virulence and possibly vertical transmission of pathogens. The nutrition-immunity-infection model is, therefore, more complex than originally thought (*Harbige and Gershwin, 2004*).

Protein – energy malnutrition in young children increased their susceptibility to common childhood illness such as diarrhea and acute respiratory infections which, in turn, increased their risk of being undernourished as a result of reduced food intake and increased losses from poor absorption and metabolism. Over the last 30 years, considerable progress has been made in understanding the mechanisms by which undernutrition – and more recently specific micronutrient deficiencies – can affect the immune system and thus the response to infections (*Ramakrishnan et al, 2004*).

Functional foods as a term is used to describe foods fortified with ingredients capable of producing health benefits. Probiotic products represent a strong growth area within the functional foods group. Such probiotic foods, especially dairy products such as yogurts and fermented milks, may modulate gut microbial composition, thereby leading to improved gut health, for example, through improved tolerance to lactose in lactose – intolerant individuals or improved resistance to pathogenic bacteria (*Stanton et al*, 2001).

The interrelation of nutrients and skin, particularly the photoprotective effects of vitamins, carotenoids, and polyunsaturated fatty acids, is well known. Supplementation with these nutrients was shown to provide protection against ultraviolet light and influences cutaneous immune responses. Dietary consumption of certain plants or fish oil is known to modulate the balance of lipid inflammatory mediators and, therefore, is valuable in the treatment of inflammatory skin disorders (*Boelsma et al*, 2001).

## AIM OF THE WORK

This essay reviewed selected types of foods, and micronutrients and their known functions in the complex immune system.