

THE LABORATORY INSIGHT INTO AGE-RELATED DISEASES AND ANTI-AGING MEDICINE

Essay

Submitted for Partial Fulfillment of
Master Degree in Clinical and Chemical Pathology

By

Menat Allah Ali Mahmoud Shaaban

(M. B., B. Ch.)

Ain Shams University

Supervised by

Dr. Nashwa Ahmed Adel El- Badawi

Professor of Clinical and Chemical Pathology

Faculty of Medicine, Ain Shams University

Dr. Perihan Hamdy Tawfik

Professor of Clinical and Chemical Pathology

Faculty of Medicine, Ain Shams University

Dr. Abeer I. Abd El Mageed

Lecturer of Clinical and Chemical Pathology

Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University

2006

الرؤية المعملية حول الطب المضاد للأمراض المصاحبة لتقدم السن

رسالة توطئة للحصول علي درجة الماجستير في الباثولوجيا
الإكلينيكية و الكيميائية

مقدمة من

الطبيبة/ منة الله علي محمود شعبان
بكالوريوس الطب و الجراحة- كلية الطب- جامعة عين شمس

تحت إشراف

ا.د./ نشوي أحمد عادل البدوي
أستاذ الباثولوجيا الإكلينيكية و الكيميائية
كلية الطب- جامعة عين شمس

ا.د./ بريهان حمدي توفيق
أستاذ الباثولوجيا الإكلينيكية و الكيميائية
كلية الطب- جامعة عين شمس

د./ عبير إبراهيم عبد المجيد
مدرس الباثولوجيا الإكلينيكية و الكيميائية
كلية الطب- جامعة عين شمس

كلية الطب
جامعة عين شمس

٢٠٠٦

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
وَ قُلْ اَعْمَلُوا فَسَيَرَى اللَّهُ
عَمَلَكُمْ

وَ رَسُولُهُ وَ الْمُؤْمِنُونَ
صَدَقَ اللَّهُ الْعَظِيمِ

Acknowledgement

First of all, thanks to ALLAH who provides me, with his unlimited generosity, the medical knowledge which I hope to be a benefit for people and provides me the strength to complete this work.

It is a great honor to express my sincere gratitude and deep appreciation to ***Dr. Nashwa Ahmed Adel El Badawi***, Professor of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, who gave me the honor of working under her remarkable supervision that makes me really fortunate and who was kind to offer me much of her valuable time, sincere advice and valuable experience.

I would like to express my sincere gratitude and deep respect to ***Dr. Perihan Hamdy Tawfik***, Professor of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for her extra-ordinary help, remarkable advice, close supervision, unimaginable efforts and continuous encouragement which had a basic role in the completion of this work.

I would like to express my sincere gratitude and deep respect to ***Dr. Abeer Ibrahim Abd El Mageed***, Lecturer of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University for her patience, contact supervision, valuable suggestions and guidance which had an obvious contribution in accomplishing this work.

Finally, I can not fully express by any words my deep gratitude to my dear parents, my beloved sister and brother who I owe a lot and to whom I dedicate this work.

List of Abbreviations

ACTH	Adrenocorticotrophic hormone
AFP	Alpha fetoprotein
AFU	α -L-fucosidase
Apo-A	Apolipoprotein A
Apo-B	Apolipoprotein B
ATP	Adult Treatment Panel
BAP	Bone-specific alkaline phosphatase
BMD	Bone mineral density
BMI	Body mass index
BRCA I-II	Breast cancer susceptibility genes I-II
BSP	Bone sialoprotein
BT	Bioavailable testosterone
cFT	Calculated free testosterone
CHD	Coronary heart disease
CRP	C-reactive protein
CTx	Collagen type I crosslinked carboxyl terminal peptide
CVD	Cardiovascular disease
DCBE	Double contrast barium enema
DEXA	Dual-Energy X-ray Absorptiometry
DHEA	Dehydroepiandrosterone
DHEAS	Dehydroepiandrosterone sulphate
DHT	Dihydrotestosterone
DNA	Deoxyribonucleic acid
DPD	Deoxypyridinium
DRE	Digital rectal examination
ELISA	Enzyme-linked immunosorbent assay
FAI	Free androgen index
FHS	Framingham Heart Study
FIT	Fecal immunochemical test
FOBT	Fecal occult blood test
FPG	Fasting plasma glucose

FSH	Follicle stimulating hormone
FT	Free testosterone
GnRH	Gonadotropin-releasing hormone
GH	Growth hormone
GHRH	Growth hormone-releasing hormone
HbA1c	Hemoglobin A1c
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HDL-C	High density lipoproteins-cholesterol
HPA	Hypothalamic-pituitary adrenal axis
2hPG	2-hours plasma glucose
HRT	Hormone replacement therapy
hs-CRP	High- sensitivity C-reactive protein
IDL-C	Intermediate density lipoproteins-cholesterol
IFG	Impaired fasting glucose
IFN-α	Interferon-alpha
IGF-I	Insulin-like growth factor-I
IGFBP	Insulin-like growth factor binding protein
IGT	Impaired glucose tolerance
LDL-C	Low density lipoproteins-cholesterol
LH	Leutinizing hormone
Lp(a)	Lipoprotein(a)
MMAS	Massachusetts Male Aging Study
MWHS	Massachusetts Women's Health Study
NCEP	National Cholesterol Education Program
NGT	Normal glucose tolerance
NHANES	Third National Health and Nutrition
III	Examination Survey
NTx	Collagen type I cross-linked amino terminal peptide
OC	Osteocalcin
OGTT	Oral glucose tolerance test
ORAC	Oxygen radical absorbance capacity

OSS	Oxidative stress status
PADAM	Partial Androgen Deficiency in Aging Males
PICP	Procollagen type I C-terminal propeptide
PINP	Procollagen type I N-terminal propeptide
proPSA	Precursor forms of PSA
PSA	Prostate-specific antigen
RIA	Radioimmunoassay
RPSA	Ratio of FPSA to TPSA
ROS	Reactive oxygen species
rT₃	Reverse T ₃
SD	Standard deviation
SHBG	Sex hormone binding globulin
SWAN	Study of Women's Health Across the Nation
T₃	Tri-iodothyronine
T₄	Tetraiodothyronine
TAC	Total antioxidant capacity
TEAC	Trolox equivalence antioxidant capacity
TPO	Thyroperoxidase
TPSA	Total PSA
TRAcP	Tartrate-resistant acid phosphatase
TRH	Thyrotropin releasing hormone
TRT	Testosterone replacement therapy
TSH	Thyroid stimulating hormone
USPSTF	U.S. Preventive Services Task Force
VEGF	Vascular endothelial growth factor
VLDL-C	Very low density lipoproteins-cholesterol
WHO	World Health Organization

List of Figures

		Page
Figure (1)	Glucose homeostasis: roles of insulin, glucagon, amylin, and glucagon-like peptide-1.	27
Figure (2)	Hormonal changes during the female reproductive cycle.	33
Figure (3)	Hormone feedback control in the female reproductive cycle.	34
Figure (4)	Physiological changes of female sex hormones with aging.	35
Figure (5)	Control of testosterone secretion.	45
Figure (6)	Adrenal cortical hormones synthesis.	53
Figure (7)	The hypothalamic-pituitary-adrenal (HPA) feedback system that regulates glucocorticoids (cortisol) levels.	54
Figure (8)	Age-related changes in dehydroepiandrosterone (DHEA) level.	56
Figure (9)	Control of growth hormone (GH) secretion.	59
Figure (10)	Growth hormone (GH) decline with age.	61
Figure (11)	Thyroid hormones regulation.	65
Figure (12)	Melatonin molecule.	70
Figure (13)	Age-related decline in melatonin level.	72

List of figures

Figure (14)	Biochemical markers of bone remodeling.	82
Figure (15)	High-sensitivity C-reactive protein adds prognostic information on vascular risk at all levels of the Framingham Risk Score and all levels of low-density lipoprotein – cholesterol.	95

List of Contents

• LIST OF ABBREVIATIONS	i
• LIST OF TABLES	iv
• LIST OF FIGURES	vi
• LIST OF FLOWCHARTS	viii
• INTRODUCTION AND AIM OF THE WORK	1
• REVIEW OF LITERATURE	
Chapter I: AGING PROCESS	3
A- Definition of Aging	3
B- Characteristics of Aging	4
C- Relationship Between Aging and Disease ..	4
D- The Gender Difference and Longevity	5
E- Theories of Aging	6
Chapter II: DISTURBANCES IN PHYSIOLOGICAL	
SYSTEMS WITH AGING	
A- Osteoporosis	11
B- Cardiovascular Disease	13
C- Type 2 Diabetes Mellitus	24
D- Hormonal Disturbances	30
1- Female sex hormones	30
2- Male sex hormones	44
3- Adrenal hormones	52
4- Growth hormone	58
5- Thyroid hormones	64
6- Melatonin	70
E- Oxidative stress	74

Chapter III: LABORATORY SCREENING AND MANAGEMENT FOR ANTICIPATED DISORDERS OF AGING

A- Osteoporosis	79
B- Cardiovascular Disease	87
C- Type 2 Diabetes Mellitus	101
D- Hormonal Screening and Supplementation Therapy	104
1- Female sex hormones	104
2- Male sex hormones	107
3- Adrenal hormones	114
4- Growth hormone	116
5- Thyroid hormones	119
6- Melatonin	125
E- Cancer	129
1- Association between aging and cancer ..	129
2- Guidelines for early detection of cancer	129
3- The role of serum tumor markers in cancer screening	132
a- Testing for early breast cancer detection	133
b-Testing for early colorectal cancer detection using fecal occult blood test	135
c- Testing for early prostate cancer detection using prostate-specific antigen	137
d- Testing for early ovarian cancer detection using CA125	139
e- Testing for early hepatocellular carcinoma detection	142

f- Recent advances in cancer screening	145
F- Oxidative Stress	147
• SUMMARY AND CONCLUSION	152
• RECOMMENDATIONS	156
• REFERENCES	158
• ARABIC SUMMARY	

List of Flowcharts

		Page
Flowchart (1)	Scheme for diagnosis and management of osteoporosis	86
Flowchart (2)	An algorithm for lipid management in adults	99
Flowchart (3)	Scheme for androgen deficiency screening	111
Flowchart (4)	Scheme for management of subclinical hypothyroidism	122
Flowchart (5)	Scheme for management of subclinical hyperthyroidism	124

List of Tables

		Page
Table (1)	Comparison of peak concentrations of hormones in premenopausal, perimenopausal and postmenopausal women.	38
Table (2)	Age-related changes in sex hormone binding globulin (SHBG) level in women.	43
Table (3)	Age-related changes in testosterone, free androgen index (FAI), calculated free testosterone (cFT) and sex hormone binding globulin (SHBG).	47
Table (4)	Effects of androgen deficiency identified by the Second Andropause Consensus Meeting, compared to normal aging.	50
Table (5)	Age-related changes in cortisol level.	57
Table (6)	Age-related changes in insulin –like growth factor-I (IGF-I) with age.	63
Table (7)	Studies of diagnostic accuracy of markers to predict bone loss	83
Table (8)	Biomarkers for identifying the coronary heart disease vulnerable patient.	87
Table (9)	Adult treatment panel III classification of LDL, total and HDL-Cholesterol.	90
Table (10)	Framingham point system for men.	92
Table (11)	Framingham point system for women.	93

List of tables

Table (12)	LDL-Cholesterol goals and cutoff points for therapeutic life changes and drug therapy in different risk categories.	94
Table (13)	Recommendations of eight organizations regarding screening of asymptomatic adults for thyroid dysfunction.	120
Table (14)	American Cancer Society recommendations for the early detection of cancer in average-risk asymptomatic people.	130