DIABETIC AUTONOMIC NEUROPATHY

Thesis
Submitted to the Faculty of Medicine
Ain Shams University
In Partial Fulfilment of the Requirements
for Master Degree of

GENERAL MEDICINE

By

Roushdy Henein Saad

(M B B Ch, Alex)

R. H

SUPERVISORS :

Prof Dr Samir Sadek,

Professor of General Medicine;

Ain Shams University

Dr Fadila Gadalla,

Lecturer of General Medicine;

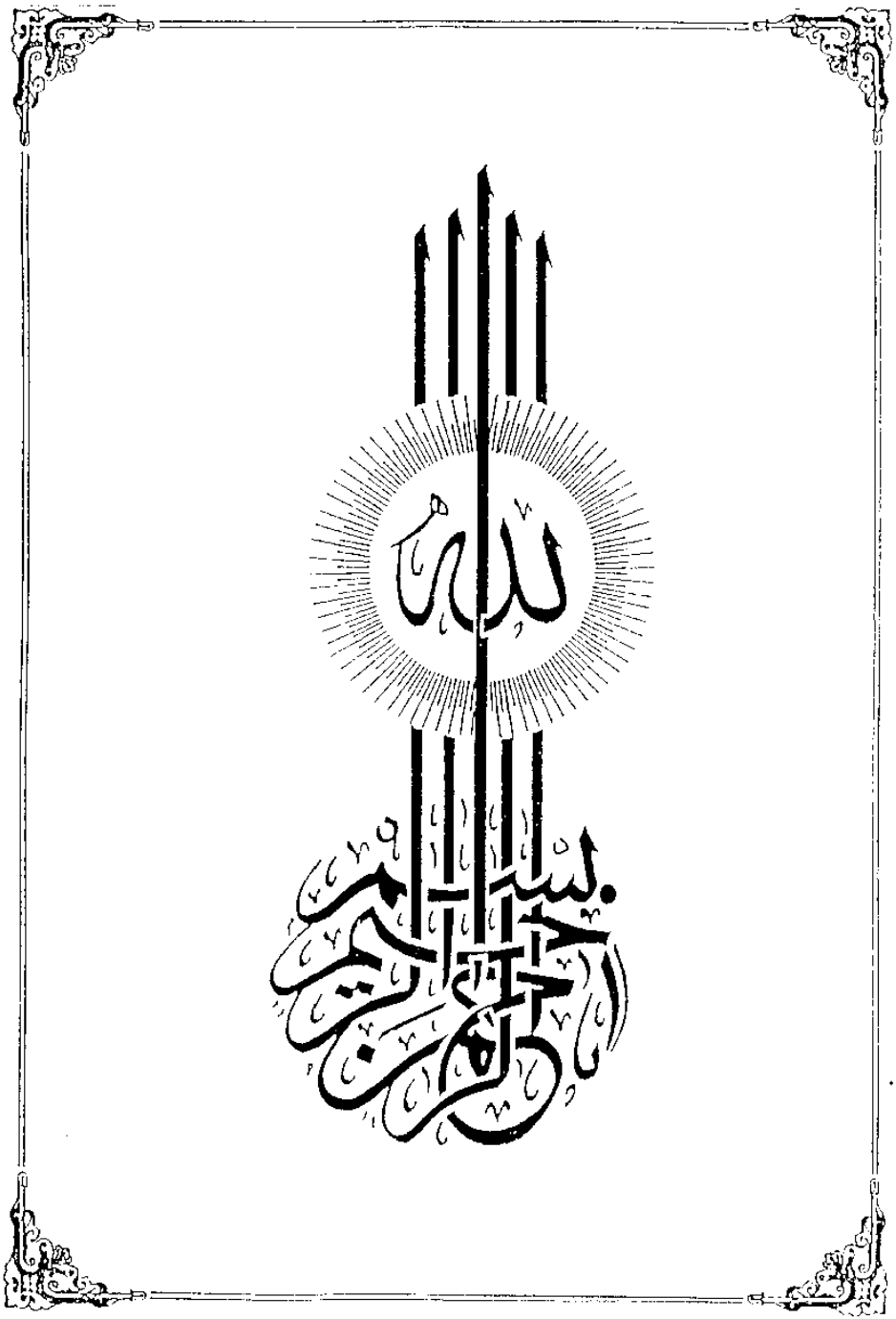
Ain Shams University

FACULY OF MEDICINE

AIN SHAMS UNIVERSITY

1987

CONTENTS



ACKNOWLEDGEMENT

It is a great pleasure to express my deepest gratitude and cordial appreciation to: Professor Doctor: SAMIR SADEK for suggesting and supervising the present work, for his continuous guidance and encouragement and for his continuous advise. I will remain always remembering.

Also, I am deeply indebted to: Doctor: FADILA GADALLA who was alawys encouraging and was a faithful guide, who aroused my interest in the subject.

I gratefully wish to thank Professor Doctor : ABOU-MAATY N. AHMED, the head of the Edocrine Unit, where I worked, I will always remember.

Furthermore, I would like to express my best feelings and sense of gratitude to all my other colleagues; for their sincere co-operation, and to all who helped me in this work.

Also my thanks to the patients and volunteers who gave their time to answers my questions.

Finally, I am deeply indebted to my mother for her continuous encouragement and support.

AIM OF THE WORK

AIM OF THE WORK

The aim of this work is to evaluate the autonomic neuropathy in forty diabetic patients in correlation with DURATION and TYPE of diabetes mellitus by different parameters seen in outpatient clinics or admitted to medical wards.

Recently, several simple methods for qualitative estimation of autonomic nervous system abnormalities have been published, most of which were based upon measurement of variation in heart rate beat to beat under different conditions by simple non-invasive bed side tests in Insulin-dependent and Non Insulin-dependent diabetic patients of short and long duration of diabetes mellitus.

INTRODUCTION

INTRODUCTION

DEFINITION OF: DIABETES MELLITUS AND PERIPHERAL NEUROPATHY:

DIABETES MELLITUS is a heterogenous primary disorder of carbohydrate metabolism with multiple etiological factors that generally involve absolute or relative insulin deficiency or insulin resistance or both. All causes of diabetes ultimately lead to hyperglycemia which is the hallmark of this disease syndrome.(1) Diabetic syndrome consists of a metabolic, vascular and neurological components, the metabolic component is charactertized by inappropriate elevation of blood glucose level accompanied with alteration in lipid and protein metabolism, the vascular component consists of accelerated non-specific atherosclerosis and a more specific microangiopathy particularly affecting the eye and the kidney.(2)

PERIPHERAL NEUROPATHY is defined as "deranged function and structure of peripheral motor, sensory and autonomic neurons, invloving either the entire neuron or selected levels". The disorder can appear clinically in diverse ways, depending on the severity of the process, the rate of progression, the anatomic structures affected, the population of neurons or shwann cells affected, the level within the neurons affected and the subcellular pathologic process involved.(3)

ANATOMY AND ORGANIZATION AND PHYSIOLOGY of the Autonomic Nervous System

The autonomic nervous system regulates the functions of smooth muscles, the heart and glands. It is composed of two majors divisions, termed sympathetic and parasympathetic, which are anatomically, physiologically, and biochemically quite distinct. Activation of the sympathetic system leads to the classic "flight or fight" responses of tachycardia, increased force of cardiac contraction, vasoconstriction, mydriasis, bronchodilatation, and hyperglycemia. Parasympathetic nervous activity results in a situation better examplified by an "old man sleeping after dinner", with slow heart rate, noisy respirations (caused by bronchial constriction), meiosis, and saliva running out of the corner of his mouth. Auscultation of the abdomen would reveal loud bowel sounds.

ANATOMICALLY, the "sympathetic nervous system" is composed of pathways that originate from neurons with cell bodies in the "thoracolumbar" segments of the spinal cord. These segments give preganglionic neurons where synapse in the sympathetic ganglia with postganglionic neurons, which in turn innervate endorgans, including vascular, gastrointestinal,

and genitourinary smooth muscle and the heart.

BY CONTRAST , the "parasympathetic pathways" originate from neurons that have their cell bodies in the "craniosacral" portions of the neuraxis, including the midbrain, the medulla and the sacral portions of the spinal cord. Preganglionic fibres synapse in peripheral ganglia that are in general closure to innervated organs than is the case with the sympathetic system.

Communications between neurons in the autonomic nervous system, and between neurons and effector cells, is mediated by chemicals called neurotransmitters. Acetylcholine encodes communication between preganglionic and postganglionic neurons in both the sympathetic and parasympathetic nervous systems.

Norepinephrine is generally the neurotransmitter at sympathetic postganglionic nerve endings, whereas acetylcholine is the transmitter at parasympathetic postganglionic nerve endings.(4)

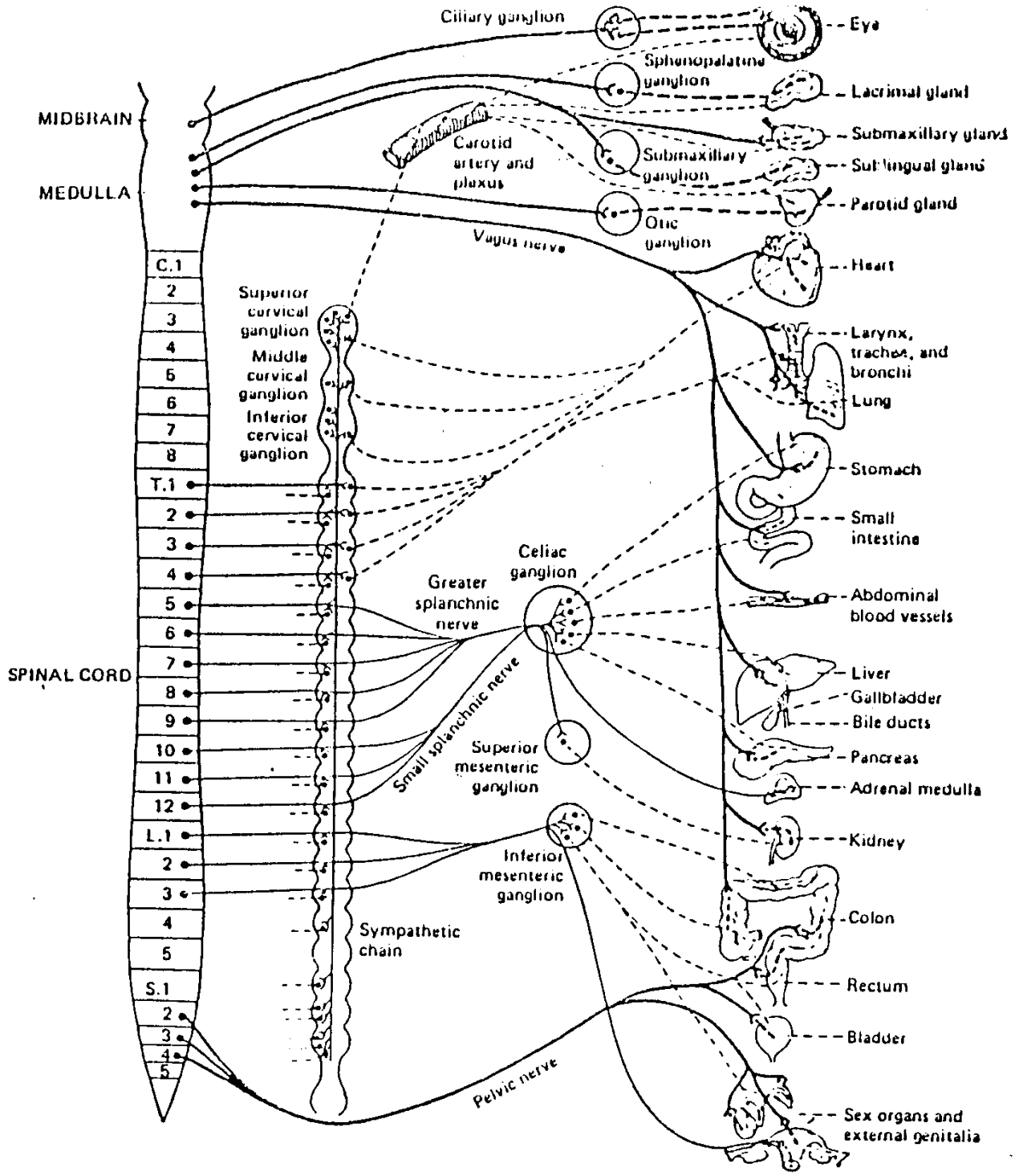


Figure 13–2. Diagram of the efferent autonomic pathways. Preganglionic neurons are shown as solid lines, postganglionic neurons as dashed lines. The heavy lines are parasympathetic fibers; the light lines are sympathetic. (Modified and reproduced, with permission, from Youmans W: *Fundamentals of Human Physiology*, 2nd ed. Year Book, 1962.)

CHEMICAL TRANSMISSION
in the Autonomic Nervous System

ACETYLCHOLINE is stored in clear vesicles in the synaptic terminals of cholinergic neurons. It is released from the terminals by the nerve impulses. The secreted A.ch. is in turn hydrolysed by the enzyme acetyl choline esterase and the enzyme choline acetylase on the other hand catalyses the synthesis of acetylcholine from choline and active acetate. The stimulator effects of acetylcholine on smooth muscles and glands mimics the stimulatory action of muscarine, therefore called "muscarinic actions" and the receptors are muscarinic receptors, blocked by atropine. In sympathetic ganglia, small amounts of A. ch. stimulate postganglionic neurons and large amounts block transmission of impulses from pre- to postganglionic neurons. These actions are unaffected by atropine but mimicked by nicotine, consequently, these actions of A. ch. are nicotinic actions and the receptors are nicotinic receptors.

The chemical transmitter NOREPINEPHRINE is stored in the synaptic knobs of adrenergic neurones in characteristic granules. Adrenergic neurons has multiple varicosities

along its course, and each of these varicosities appears to be a site at which norepinephrine is liberated.

On the basis of the chemical mediator released, the autonomic nervous system can be divided into cholinergic and adrenergic divisions.

The neurones which are cholinergic are, all preganglionic neurons, the anatomically parasympathetic postganglionic neurons and the anatomically sympathetic postganglionic neurons which innervate the sweat glands the anatomically sympathetic neurons which end on blood vessels in skeletal and produce vasodilatation when stimulated. The remaining postganglionic sympathetic neurons are adrenergic.(5)

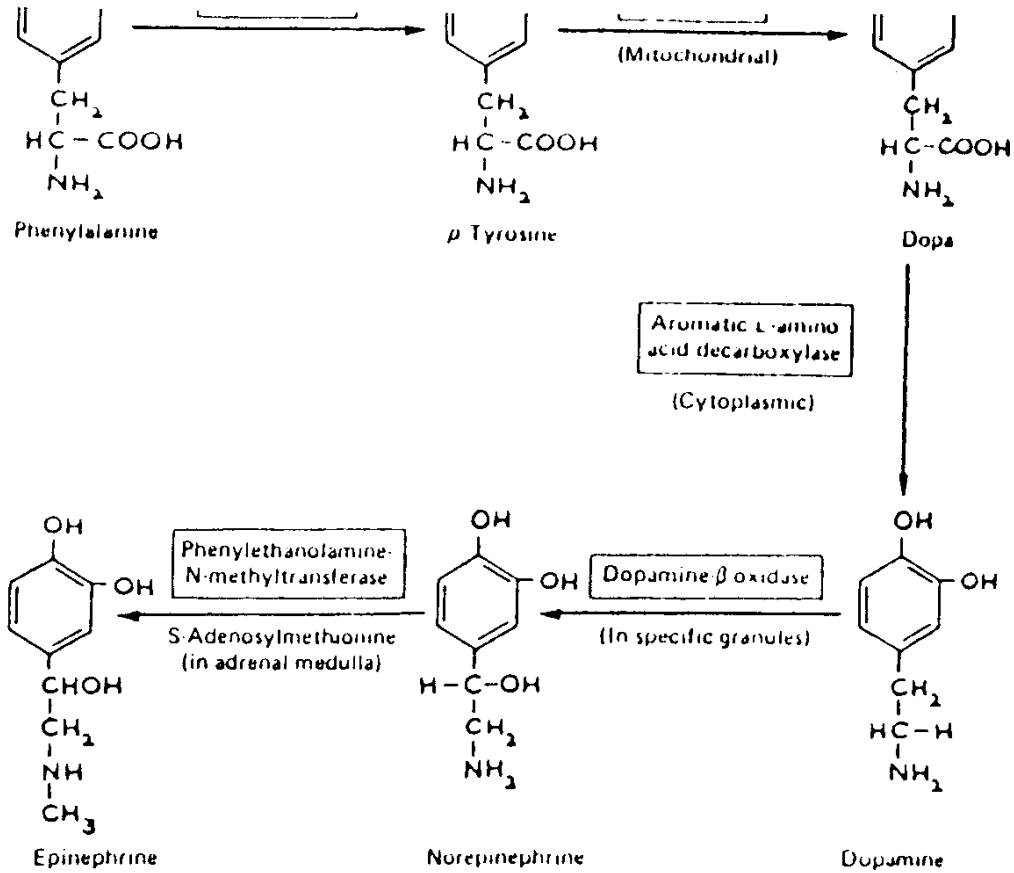


Figure 4–3. Biosynthesis of catecholamines. Dopa, dihydroxyphenylalanine; dopamine, dihydroxyphenylethylamine. (Modified and reproduced, with permission, from Meyers FH, Jawetz E, Goldfien A: *Review of Medical Pharmacology*, 7th ed. Lange, 1980.)

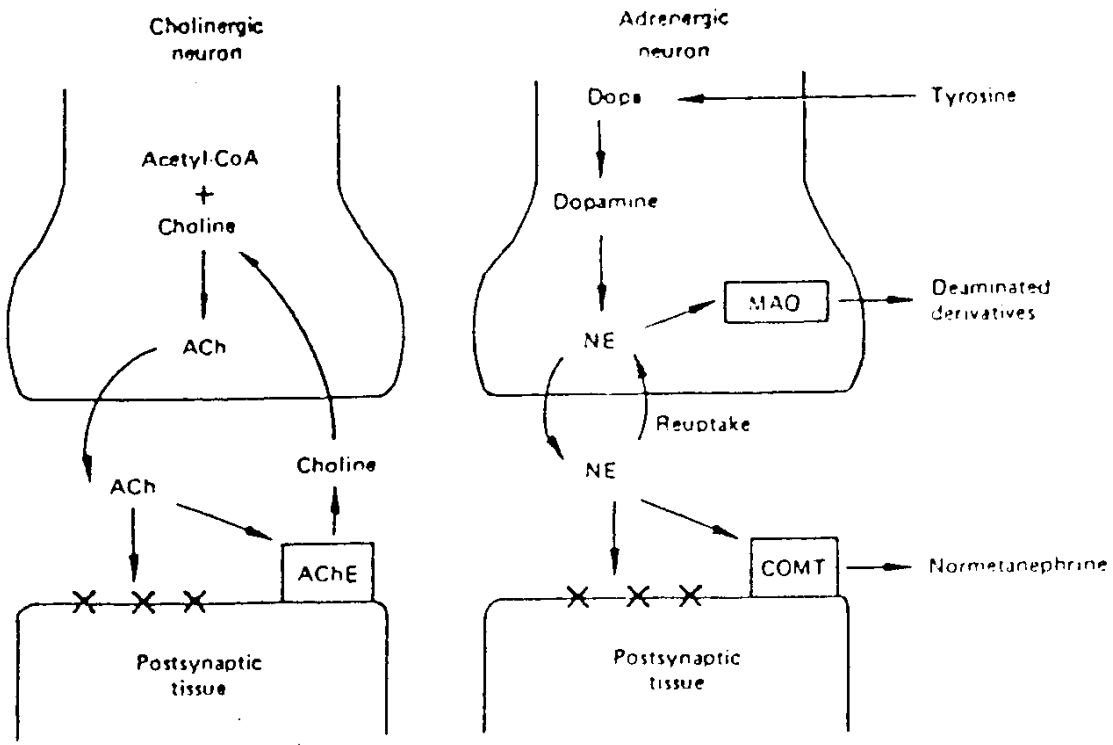


Figure 4–2. Comparison of the biochemical events at cholinergic endings with those at adrenergic endings. ACh = acetylcholine; AChE = acetylcholinesterase; NE = norepinephrine; X = receptor. Note that monoamine oxidase (MAO) is intracellular, so that some norepinephrine is being constantly deaminated in adrenergic endings. Catechol O-methyltransferase (COMT) acts on norepinephrine after it is secreted. (Reproduced, with permission, from Ganong WF: *Review of Medical Physiology*, 10th ed. Lange, 1981.)