ANESTHESIA IN GENETIC AND METABOLIC DISEASES

Essay

Submitted in partial fulfilment for

The Master Degree

in Anesthesiology

by

TAREK EL SAYED EZ EL-ARAB

M.B., B.Ch.

Supervised by

Prof. Dr. MOHAMED ABD EL- FATTAH EL-SAKKA

Professor of Anesthesiology

Faculty of Medicine

Ain Shams University

Dr. MOHAMED ABD EL- GALIL A. SALLAM

Ass. Professor of Anesthesiology

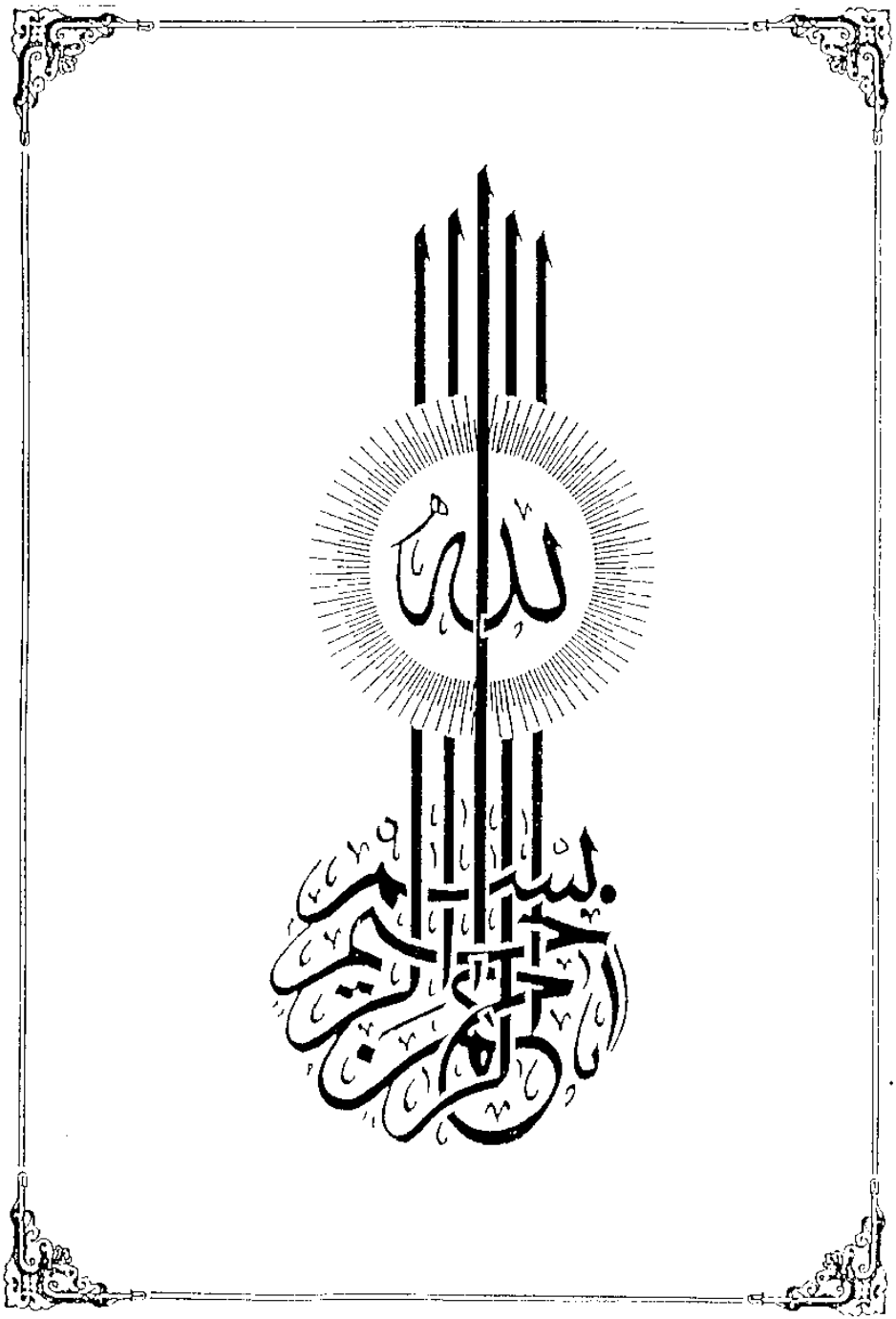
Faculty of Medicine

Ain Shams University

Faculty of Medicine

Ain Shams University

1992



ACKNOWLEDGEMENT

I would like to express my sincere gratefulness and thankfulness to prof.Dr. Mohamed El Sakka, professor of anesthesiology,Ain Shams University for his kind supervision and understanding help in accomplishing this work.

I feel deeply indebted and grateful to Dr. Mohamed A. Sallam,Assist. professor of anesthesiology Ain Shams University for his fruitful advise and continuous encouragement throughout the preparation and fulfilment of this work.

My thanks also extend to all the members of the anesthesia department and to my collegues whose help have always been invaluable.

Tarek El-Sayed

CONTENTS

INTRODUCTION

INTRODUCTION

The central roles of the anesthesiologist are to protect the patient from the pain and stress of surgical intervention and to preserve physiological homeostasis during the perioperative period. So,a knowledge of the pathophysiology of co-existing disease regardless of the reason for surgery and an understanding of concomitant drug therapy are mandatory.

The genetic and metabolic diseases are among the most exciting and challenging disorders for the specialist to deal with. The number of known metabolic diseases have increased rapidly in the recent years and they are now recognized as an important causes of disease in the pediatric age group.

The factors account for the increased recognition that these diseases are important part of medicine;

I- the greater appreciation of clinical signs of

these disorders,

2- the increased availability of reliable methods for detecting and measuring biochemical substances in physiologic fluids,

3- the emergence of newborn screening for metabolic disorders as a routine procedure that identifies biochemical disorders in infants who may be clinically normal and in whom timely treatment will prevent clinical manifestations.

The excitment surrounding the metabolic diseases have been generated by the recognition that a number of them can be treated and irriversible clinical complications prevented. So, a thorough knowledge of these diseases is essential so that optimal care can be offered to these patients throughout the perioperative period by anesthesiologist.

FUNDAMENTALS OF GENETIC SYSTEM

FUNDAMENTALS OF GENETICS

Inherited characteristics are carried from generation to generation by the chromosome, a complex nucleic acid structure in the nucleus of the cell. Humans normally have 46 chromosomes, which are arranged in 23 pairs. One of these pairs determines the sex of the individual; these are the sex chromosomes X and Y. Females have the pair XX and males have the pair XY. The remaining 22 pairs are called autosomes.

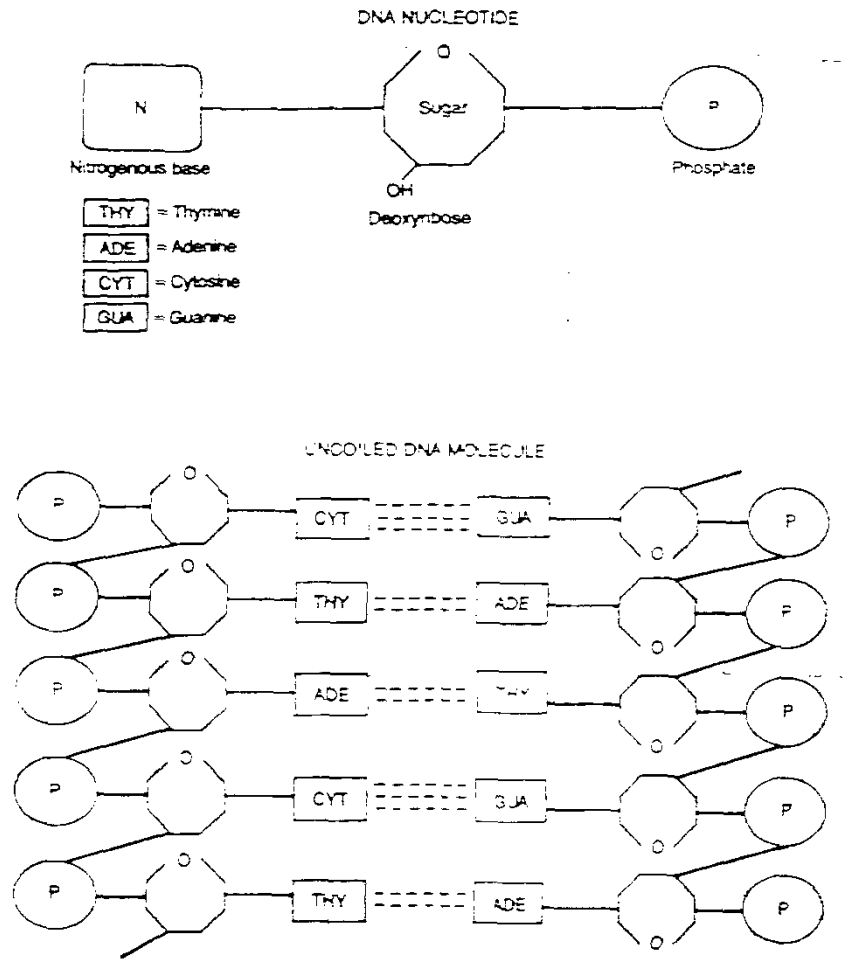
Pairs of autosomes are homologous i.e. each pair has the same configuration and constituent genetic loci as the other.

Chromosomes are composed of thousands of genes, which are the basic units of heridity. The gene is the information area for the transmission of an inherited trait. These are arranged in a linear fashion on the chromosome. The exact location of a gene on a chromosome is its locus. Each chromosome has thousands of loci arranged

in a definite manner and the number and the arrangement of genes on homologous chromosomes are identical. Genes that occupy homologous loci are alleles,or partner genes. Each individual therefore has 2 of each kind of gene,one on each chromosome of a pair of chromosomes (Kosek,I986).

THE CHEMICAL BASIS OF HERIDITY:

Each gene consists of about I500 linked molecules of deoxyribonucleic acid (DNA). Each molecule of DNA consists of two out of four possible basis linking molecules of a pentose sugar and phosphate (see figure I). The four possible basis are adenine(A), thymine(T),cytosine(C)and guanine(G) . Adenine is always paired with thymine and cytosine with guanine,but as the order of pairs down the complete structure is significant,adenine-thymine has a different significance to thymine-adenine. There are thus four possible pairs. A sequence of three such



Schematic representation of DNA nucleotide and uncoiled DNA molecule.

Fig.I (After Jackson,1990)

base pairs (called a codon) is necessary to encode for the structure of each amino acid and each gene therefore consists of about 500 such codons which are the order of magnitude of the number of amino acids in a polypeptide chain (McKusick,I979).

The information which is encoded in the genes is replicated at the time of normal cell division because each DNA molecule divides between the two bases,and each temporarily freed base attracts its complementary partner base from the substrate and this results in the reconstitution of two identical DNA molecules (Vickers and Johns,I989).

The information inherited in each gene is determined by the sequence of bases in the nucleotide. A structural gene indirectly specifies (encodes) the amino acid sequence of a polypeptide (proton)initially by transferring its genetic information (nucleotide base sequence) to a

messenger ribonucleic acid (RNA) as each DNA codon first codes a complementary RNA codon. Thus DNA may serve as a template not only for replication of DNA but also for the formation of RNA (transcription) (Haris,1980).

RNA differs from DNA in that it substitutes ribose for deoxyribose as the sugar and replaces thymine with uracil as the pyrimidine basgand is single stranded. The messenger RNA travels from the nucleus into the cytoplasm and complexes with cytoplasmic RNA. The actual formation of peptide bonds,as each amino acid is incorporated into the peptide chain by the cistern, is facilitated by a specific transfer RNA which carries (transports) the amino acid molecule. The transfer RNA attaches briefly to the messenger RNA by means of an exposed,unpaired triplet of bases known as an anticodon,which is complementary to a messenger RNA codon for that specific amino acid (McHusick,1980).

Control or regulatory (nonstructural) genes

regulate the rate of protein synthesis,control the function of other genes,and even code the structure of RNA that regulates and determines cellular function,tissue growth and differentiation (Haris,I980).

MUTATION:

It is a change of a base pair of the DNA molecule. It will result in a triplet which codes for a different amino acid resulting in an altered protein . Therefore,the level of a particular enzyme may be reduced because it is not synthesized but has reduced activity or because its instability it is more rapidly broken down (Emery and Rimoin,I990).