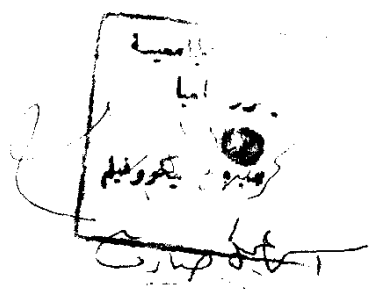
Perinatal Screening

Essay

Submitted for Partial Fulfillment of Master Degree in Pediatrics

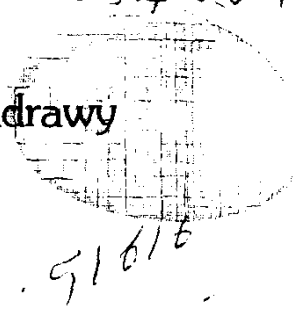
By

Amal Latif Wadie
M.B.B. Ch



Supervised by

Prof. Dr. Mohammed Fouad Badrawy
Professor of Pediatrics
Ain Shams University



Assistant Supervisor

Dr. Hisham Abdel Samie Awad
Lecturer of Pediatrics
Ain Shams University

Faculty of Medicine
Ain Shams University
1994

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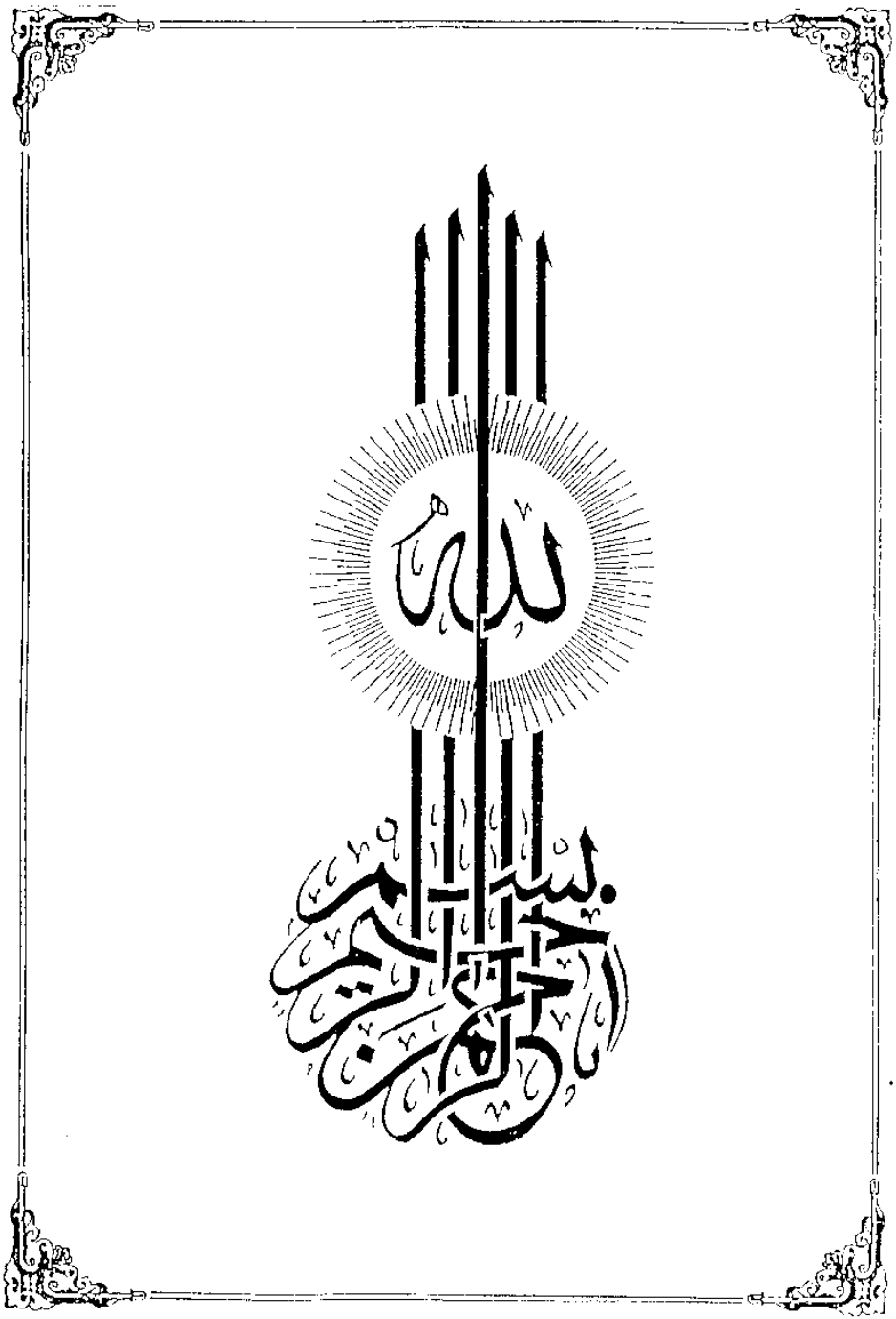
Amal Latief Wadie



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Abbreviation List

17-OHP	17 Hydroxy Progesterone
ABR	Auditory Brain-stem Response
AIDS	Acquired Immunodeficiency Syndrome
ApoB	Apolipoprotein B
ARC	Auditory Response Cradle
AV	Atrio Ventricular
BIA	Bacterial Inhibition Assay
BMD	Backer Mascular Dystrophy
CAH	Congenital Adrenal Hyperplasia
CBC	Complete Blood Count
CF	Cystic Fibrosis
CHARGE	Coloboma, congenital Heart defects, choanal Atresia, growth or mental Retardation, hypoplastic Genitalia and Ear abnormality
CK	Creatine Kinase
cM	centiMorgans
CMV	Cytomegalovirus
CNS	Central Nervous System
CPK	Creatine Phosphokinase
CSF	Cerebro Spinal Fluid
CT	Computed Tomography
CVS	Chorionic Villus Sampling
DEAFF	Detection of Early Antigen Fluorescent Foci
DMD	Duchenne Muscular Dystrophy
DNA	Deoxyribonucleic Acid
DPOAE	Distortion Product of Atoacoustic Emissions
EBV	Epstein-Barr Virus
EDS	Ehlers-Danlos Dystrophy
EIA	Enzyme Immunoassay
ELISA	Enzyme Linked Immunosorbant Assay
FTA - ABS	Fluorescent Treponemal Antibody absorption
FVW	Flow Velocity Wave form
Hb	Hemoglobin
HBsAg	Hepatitis B surface Antigen
HBV	Hepatitis B Virus
HDL	High Density Lipoprotein
HIV	Human Immunodeficiency Virus

HLA	Human Leucocytic Antigen
HSV	Herpes Simplex Virus
IDDM	Insulin-Dependent Diabetes Mellitus
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IQ	Intelligent Quotion
IRT	Immunoreactive Trypsin
IUGR	Intrauterine Growth Retardation
M/F	Male / Female
MIE	Microvillar Intestinal Enzyme
MODY	Maturity Onset Diabetes of Youth
mRNA	messenger Ribonucleic Acid
MSAFP	Maternal Serum Alphafetoprotein
MSUD	Maple Serup Urine Disease
NF	Nerofibromatosis
NIDDM	Non-Insulin Dependent Diabetes Mellitus
OI	Osteogenesis Imperfecta
P	Plasmodium
PCR	Palymerase Chain Reaction
Pi	Protease inhibition
PKU	Phynylketonuria
PUBS	Percutaneous Umbilical Blood Sampling
RFLP	Restriction Fragment Length Polymorphism
Rh	Rhesus
RIA	Radioimmunoassay
RNA	Ribonucleic Acid
SEA	South East Asians
SGOT	Serum Glutamic Oxaloacetic Transaminase
SGPT	Serum Glutamic Pyruvic Transaminase
T4	Tetraiodothyronine
TC	Tissue Culture
TEOAE	Transitory Evoked Atoacoustic Emissions
TSH	Thyroid Stimulating Hormone
VACTERL	Vertebral malformation, imperforate Anus, Cardiac anomalies, Tracheo Esophageal festula, Renal and Limb defects

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Introduction and Aim of the Study

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Developments in DNA technology have resulted in a dramatic increase in the number of genes identified. With the localization of a gene it is possible to devise procedures suitable for mass carrier screening programs. Until recently mass carrier screening was only possible for a limited number of disorders, for example, hemoglobinopathies and Tay-Sachs disease. Counseling possible carriers was based on estimations of risk. The momentum towards mass carrier screening is likely to be increased by gene therapy.

Carrier screening for cystic fibrosis alone will have dramatic implications for genetic service provision as 4% to 5% of the UK population carry the CF gene. The potential for genetic screening of multifactorial diseases, for example, cancers, should also be considered. The existing organization of genetic services is likely to be inadequate. A new specialty of clinical population genetics is required. A model is proposed of clinical population genetic screening programs, organized under a 'common umbrella' led by a public health physician, while screening and follow up will remain the responsibility of the appropriate clinician *(Shickle and Harvey, 1993)*.

The term 'population genetics' is already used in the context of the study of the origin and dynamics of genetic variation within populations *(Waldenstrom, 1990)*. Nevertheless, we would advocate the title 'clinical population genetics' in preference to 'community genetics'. This should prevent any confusion over the location of such screening.

Clinical population genetic screening has been performed for many years, for example, neonatal phenylketonuria screening *(Medical Research Council Steering Committee, 1981)*, and prenatal screening for neural tube defects based on maternal serum α fetoprotein. Carrier screening for hemoglobinopathies *(WHO, 1983)*, is the only mass screening programs to be consistently successful outside the perinatal period. The lead specialty for each of these examples differs with a large number of departments involved: medical genetics, obstetrics, pediatrics, hematology, medical biochemistry, and general practice. Lack of cooperation and communication have

been major obstacles to the provision of multi specialty services *(Wald and Cuckle, 1984).*

The increased number of programs using the 'outwards-in' screening model means that there are advantages to having a 'common umbrella' even if the responsibility for screening and follow up remains with individual specialties. Some genetic screening programs are relatively small. Thus integration with other programs would allow exchange of experience and joint appointment of staff. As new screening programs are approved for implementation, they could be developed alongside the existing services, so facilitating a smoother introduction.

The increase in the proportion of infant deaths attributable to genetic disease, improved diagnostic techniques permitting carrier screening, together with gene therapy means that genetics represents a significant area for potential 'health gain' in the future *(Harris, 1991).* However, in view of understandable ethical concerns *(Working Group of the Royal College of Physicians Committee, 1991)*, the development of clinical population genetics will require careful consideration. The possibility of screening for 'adult diseases' during childhood will need particular attention *(Harper, 1991).* Thus, clinical population genetics should be clearly defined, with aims and objectives to allow evaluation and a formal structure which demands evidence of benefit before investment occurs. The model described of an 'umbrella' structure managed by public health physicians, covering a collection of similar screening programs using the 'outwards-in' approach, may be a way of ensuring that the promised health gain is secured.

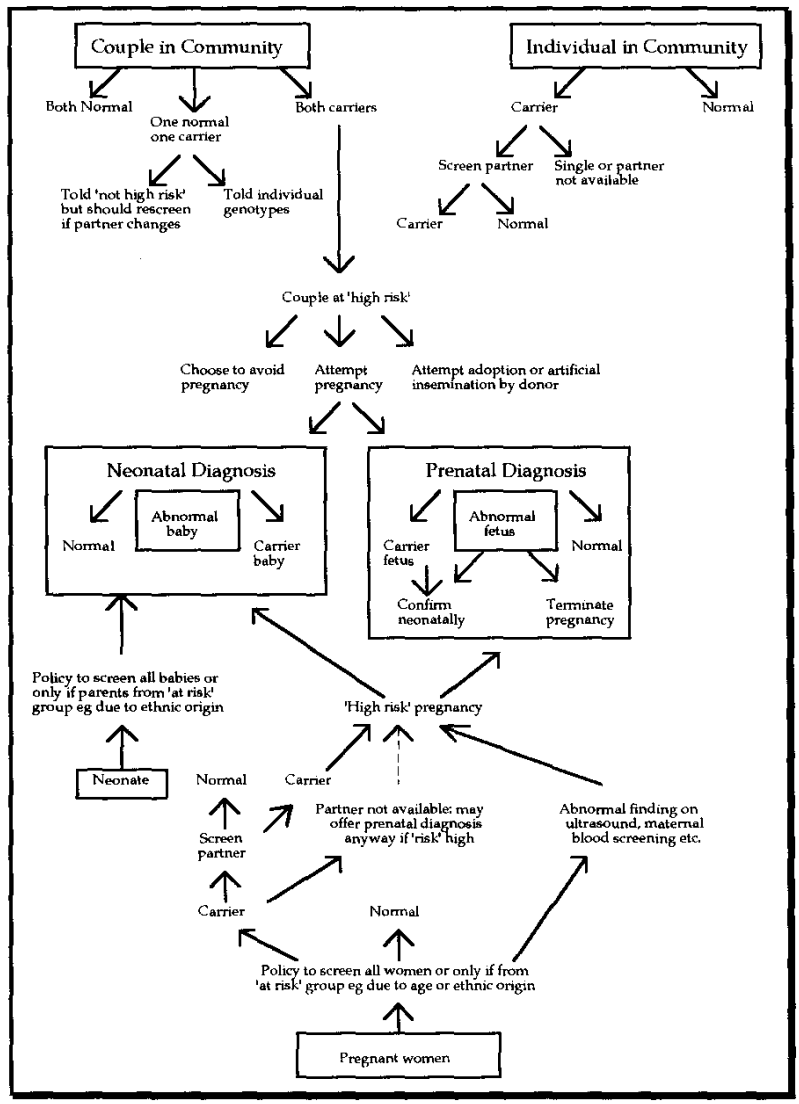

Figure 1

The 'outwards-in' model characterizes screening programs which test individual persons or couples with no previous family history of a genetic abnormality and then work 'inwards' to identify heterozygotes or homozygotes.

Prenatal Genetic Counseling

Prenatal Genetic Counseling

In 1963, Reed, first used the term genetic counseling to describe the Provision of medical information to parents regarding inherited conditions. *In 1975, the Ad Hoc Committee on Genetic Counseling,* formally defined genetic counseling as a communication process that deals with the occurrence or the risk of occurrence of a genetic disorder in a family.

In recent years, we have seen important advances in prenatal diagnostic and laboratory techniques that have broadened significantly the scope of genetic counseling for the pregnant patient. Genetic screening programs, first-trimester procedures, applied molecular genetics, and improved resolution with ultrasonography have all added new dimensions to genetic counseling. It is likely that pre-implantation diagnosis may be available soon for couples using in vitro fertilization, thus expanding the role of the prenatal genetic counselor.

The combination of these advances enables us to provide couples with more information about the well-being of their fetuses, so that they may make informed decisions regarding their reproduction.

Role of the Genetic Counselor

As a profession, genetic counseling has taken on a wide range of challenges related to the delivery of genetic health care services including, clinical educational, research, and administrative responsibilities, as well as the development and marketing of new technologies. Pregnant patients with concerns about the well-being of their fetuses represent the largest group requiring genetic counseling services. Throughout the process of prenatal diagnosis and counseling, the couple requires support in understanding and adjusting to the risks for fetal abnormalities.

By far, most women with reproductive genetic concerns are indicated for counseling because of advanced Maternal age (35 or older at delivery). The importance of a detailed pedigree, pregnancy history, and a thorough discussion of

the risks and benefits of invasive prenatal diagnostic procedures cannot be overemphasized.

The major components of the prenatal genetic counselor's role can be broken down as follows:

1. Obtaining and Interpreting the Family History

The family history is taken typically by constructing a pedigree using standard symbols and should include, at least, the first-, second-, and third-degree relatives to the fetus. The pedigree should be extended to include more distant relatives with a condition or conditions that may be familial in etiology and that potentially may affect the fetus. Information should be obtained on each individual's age or age at time of death, cause of death, presence of any birth defects, mental retardation or learning problems, sensory deficits, chronic illness, and known genetic conditions. For those of childbearing age, pregnancy losses, neonatal deaths, and infertility should be noted. If a particular condition is identified in a family member or if the couple has had a previous child with a particular condition, questions about other relatives should include the presence of minor or major features associated with the condition. The ethnic background of both the maternal and the paternal side should be noted and appropriate screening offered if indicated. Consanguinity should be noted. If the man and woman are third-degree relatives, they should be apprised of the increased risk for having a child with an abnormality. It is important to note that a negative family history does not rule out a genetic cause of a particular condition.

2. Establishment and Confirmation of a Diagnosis

An accurate diagnosis of an affected family member is central to effective genetic counseling. Review of medical records or referral to a clinical geneticist should be arranged to ensure that risks calculated are based on solid diagnostic criteria.

3. Obtaining and Interpreting the Pregnancy History

The current pregnancy history allows the assessment of teratogenic exposure, including chemicals, drugs, infection, radiation, heat exposures, or maternal disease states that impact the risk for fetal abnormalities. Additionally, a prenatal history of