LABORATORY ROLE OF CLINICAL CHEMISTRY IN NEONATAL SCREENING

ESSAY

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By

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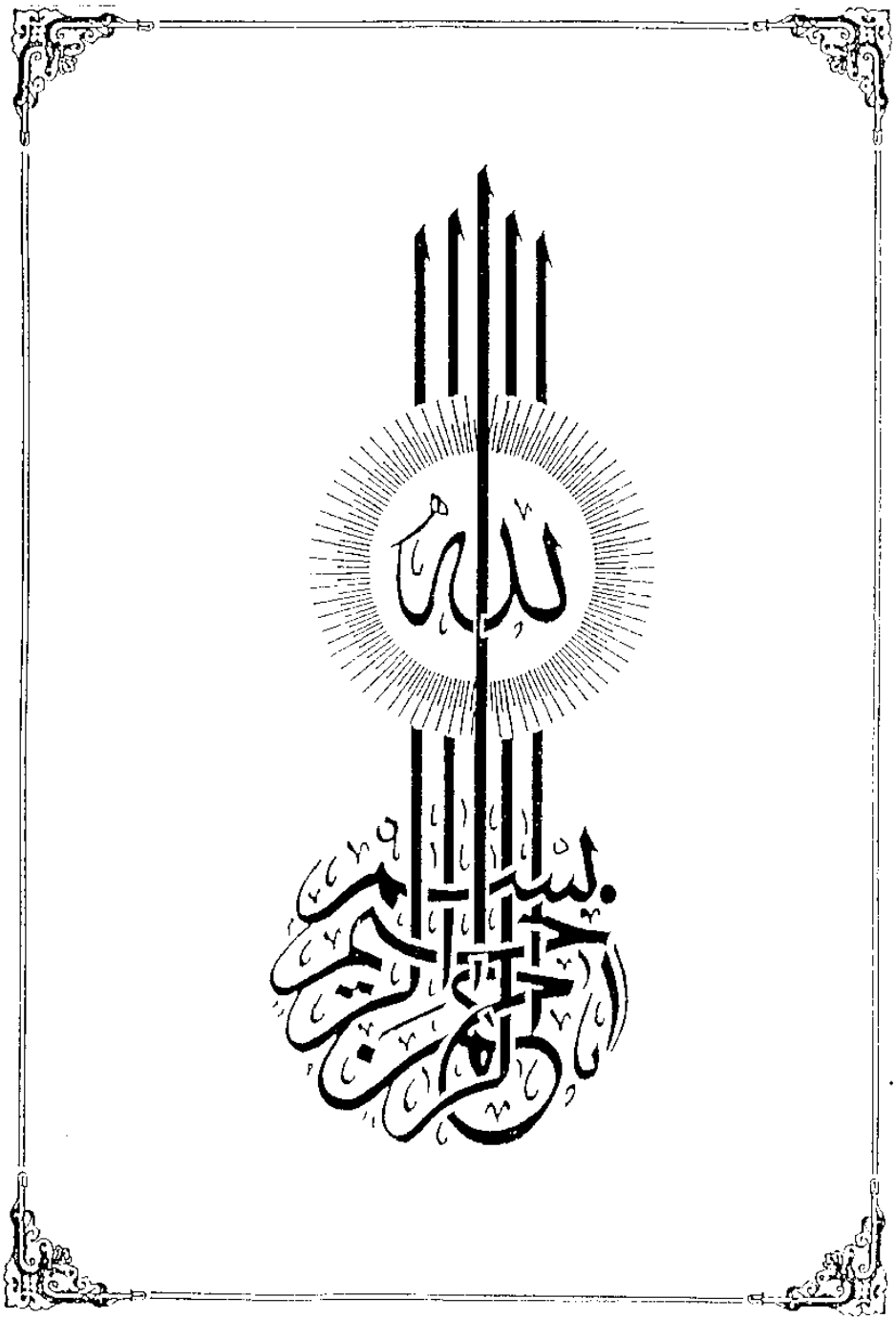

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ABBREVIATIONS

ACTH: Adrenocorticotropic hormone

AF: Amniotic fluid

ANBN: Alpha-nitroso-beta-Naphthol

AU: Arbitary unit

BH4: Tetrahydrobiopterin

BIA: Bacterial inhibition assay

3-B-HSD: 3-beta-hydroxy steroid dehydrogenase

11-B-OH: 11-beta-hydroxylase

B-PABA: N-biotinyl-para-aminobenzoic acid

CAH: Congenital adrenal hyperplasia

CF: Cystic fibrosis

CH: Congenital hypothyroidism.

CV: Coefficient variation

DNA: deoxyribo nucleic acid

DNPH: Dinitrophenylhydrazine

ELISA: Enzyme linked immunosorbent assay.

FEIA: Fluorometric enzyme immunoassay

FT_4: Free thyroxine

GALT: Galactose-1-phosphate uridyl transferase

GLC: Gas liquid chromatography

GOD: Glucose oxidase

HLA: Human leucocyte antigen

HPLC: High performance liquid chromatography

hTSH: Human thyroid stimulating hormone

INT: Iodonitrotetrazolium

IRMA: Immunoradiometric assay

IRT: Immunoreactive trypsinogen

L-BAPNA: Benzoyl-L-arginine-P-nitroanilide

LC: Liquid chromatography

MSUD: Maple syrup urine disease

NHI: Neonatal hypothyroidism index

17-OH: 17- hydroxylase

21- OH: 21-hydroxylase

21-OH-D-CAH:21-hydroxylase deficiency congenital adrenal hyperplasia.

17-OH-P: 17-hydroxy progesterone

PCR: Polymerase chain reaction

PKU: Phenylketonuria

PPA: phenylpyruvic acid

RIA: Radio-immunoassay

SD: Standard deviation

T_3: Triiodothyroxine

T_4: Thyroxine

TBG: Thyroxine binding globulin

$^{99m}TcO_4$: Technetium pertechnetate

TLC: Thin layer chromatography

TPN: Triphosphopyridine nucleotide

TSH: thyroid stimulating hormone

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Introduction:

Neonatal screening is primarily intended to screen newborn infants for disorders in which symptoms would not be clinically present until irreversible damage has occurred and for which an effective treatment would have been available. This was the basic rational utilized when screening procedures for the identification of infants with phenylketonuria or congenital hypothyroidism were introduced. In each of these disorders, affected children are asymptomatic in the early months of life and to be effective, treatment needs to be instituted in the early weeks of life ***(Irons, 1993).***

Other disorders that can be identified by neonatal screening include galactosemia, maple syrup urine disease, homocystinuria, biotinidase deficiency, tyrosinemia, cystic fibrosis as well as congenital adrenal hyperplasia ***(Buist and Tuerck, 1992).*** For these disorders, controlled long-term studies will be necessary to determine the effect of early neonatal identification and treatment of natural history of the disorder ***(Irons, 1993).***

Aim of the Work:

To discuss the different endocrinal and major metabolic disorders that can be identified by neonatal screening, to review the various laboratory tests used for their detection, to identify the more frequently occurring biochemical disorders that must be detected very early in the neonatal period and to facilitate their recognition. These are conditions

which require prompt dietary treatment to prevent irreversible neurological damage. They include those disorders that are now part of mandated newborn screening programs in many countries.

REVIEW OF LITERATURE

I) Neonatal Screening

REVIEW OF LITERATURE

I) NEONATAL SCREENING

In many countries it is now standard for every newborn infant to be tested routinely for phenylketonuria and congenital hypothyroidism. More than 50 other tests can be performed on the same obtained filter paper samples, some are in routine use, but most have not been fully evaluated for wide spread screening. In North America, all states and provinces screen for various metabolic or infectious conditions. Sometimes without regard to their incidence or public health impact ***(Buist and Tuerck, 1992).***

A- Selection of high risk baby:

The major clinical manifestations of inborn errors of metabolism in the neonatal period include; failure to thrive, poor feeding, lethargy, vomiting, diarrhea, jaundice, hypotonicity, seizures, hepatomegaly, dehydration, abnormal hair and abnormal urinary odor ***(Burton et al., 1978).***

B- Selection of screening tests:

Before a condition is considered suitable for mass screening, it should ideally meet the following criteria:

1. It should be frequent and severe enough to be a public health concern.

2. It should cause a known spectrum of symptoms.

3. The screening test should be simple and reliable and have a low incidence of false-positive and false-negative results.

4. The condition should be amenable to treatment.

5. Appropriate diagnostic tests must be readily available, and arrangements for follow up treatment should be in place.

6. There should be a positive cost-benefit ratio to society.

Few tests meet all of these criteria, the full clinical spectrum and the effect of treatment may be known for years after a test is introduced. For example, the variants of phenylketonuria and hypothyroidism were not known at the outset and there was serious debate whether early treatment would change the outcome ***(Buist and Tuerck, 1992).***

Galactosemia screening seemed to be remarkably effective by preventing early death from hepatocellular damage and gram-negative sepsis. However, a survey of 350 cases, indicated that most cases even when well diagnosed and treated, have lower IQ, speech and motor dysfunction, and growth and ovarian failure. Screening therefore, prevents death but not long term sequelae (***Waggoner et al., 1990*** and ***Buist and Tuerck, 1992).***

C- Specimen collection and handling:

1. Timing of the screening test:

Ideally, it was recommended that the screening test to be taken before hospital discharge, before 72 hours of age, and after at least 24 hours of normal protein and lactose feeding. However, such recommendations are often unattainable in the climate of early discharge. Whereas certain conditions can be detected in cord blood, others such as phenylketonuria can not be detected until some time after birth, when the intake or production rate of amino acid exceeds the infant's capacity to metabolize or excrete it. The development of hyperphenylalaninemia, therefore depends on the severity of the defect and the daily protein intake.