

SUBMITTED FOR PARTIAL FULFILLMENT
OF THE MASTER DEGREE IN PEDIATRICS

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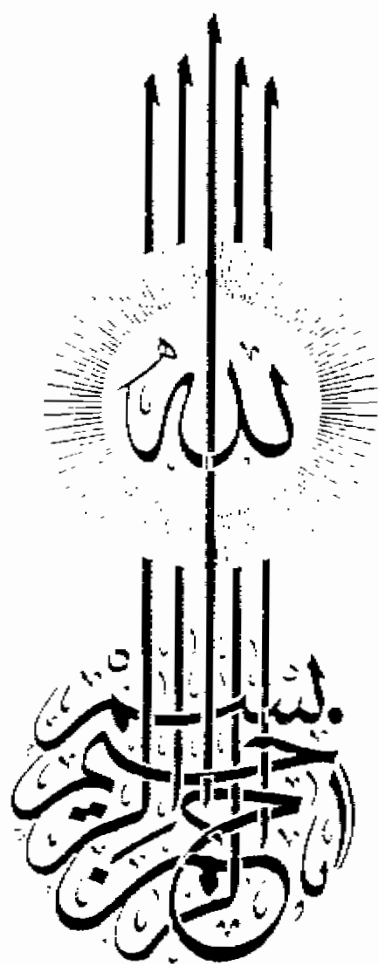
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PROF. OF PEDIATRICS

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INTRODUCTION

I. INTRODUCTION

The health of the Neonate may be affected by drugs given to his mother during pregnancy and passing to him through the placenta or by drugs given to him directly or still by drugs given to lactating mother and passing to him through milk. Accordingly, it became very essential that whenever a drug is to be given to the baby or to a pregnant or to a lactating mother, great care should be taken to determine whether that drug or its metabolites may have an adverse effect on the embryo, foetus or newborn. Its potential for harm must be carefully weighed against its potential value.

The present essay is intended to review the possible effects of drugs administered to the mother during pregnancy, parturition or lactation on the health of the newborn as well as the effect of drugs given directly to the newborn.

AIM OF THE ESSAY:

The aim of this essay is to discuss use and abuse of drugs given to mother in pregnancy or labour and of drugs given to lactating mothers or to newborns.

EFFECT OF MEDICAMENTS TAKEN BY THE PREGNANT
MOTHER ON THE NEONATAL HEALTH

II. EFFECT OF MEDICAMENTS TAKEN BY THE PREGNANT

MOTHER ON THE NEONATAL HEALTH

The mother and the conceptus can be regarded as a two-compartments model, in which the foetus is dependant in absorptive, metabolic and excretory processes on the mother.

During long term therapy, distribution equilibria are thought to exist between the two compartments, and under these conditions [sustained plasma levels of drugs] the placental "barrier" should be regarded as a relative rather than an absolute one. Metabolic conversion of drugs usually leads to formation of metabolites, which are considered to penetrate the placenta less readily than the parent compound. [Aranda et al., 1983].

The adverse effects of in utero exposure to drugs can vary from reversible effects such as transient changes in foetal breathing movements to irreversible effects such as : structural malformations, intrauterine growth retardation, mental retardation and/or foetal death.

The specific drug, the dosage, the route of administration, the timing of treatment and the genotype of the mother or the foetus, all may be critical determinants for the effect of the given drug. [Bleyer, 1970].

The timing of drug administration, has a great bearing on its effect, viz :-

- 1) The first week after fertilization is the period of zygote, during this time the common adverse effect of drugs is termination of pregnancy. [Doering and Stewart, 1978].
- 2) Exposure of the embryo during the first trimester of gestation to drugs may produce dramatic and catastrophic structural malformations.
- 3) From the third to ninth month of gestation [the period of foetal life] differentiation of the central nervous system and reproductive system continues. Drugs given during this period have been implicated as behavioural teratogens. [Aranda et al., 1983].

THE ADVERSE EFFECTS OF DRUGS GIVEN TO THE MOTHER DURING
PREGNANCY AND LABOUR :

These can be discussed from the following angles.

- A. Drugs having a teratogenic effect when given to the pregnant mother during the embryonic life [The first three months of pregnancy]. These drugs can be classified into :-
 - 1. Proved Teratogenic drugs.
 - 2. Potentially Teratogenic drugs.
- B. Drugs having an adverse effect when given to the pregnant mother during foetal life.
- C. Drugs having an adverse effect when given to the pregnant mother during labour.

A. DRUGS HAVING A TERATOGENIC EFFECT WHEN GIVEN TO THE
PREGNANT MOTHER DURING THE EMBRYONIC LIFE :

A teratogenic drug may be defined as a drug which when given during embryonic life may produce a major or minor deviation from normal morphology or function. The rapid changes in development that occur during embryonic life may cause this period to be critically sensitive to the adverse effects of drugs.

The embryonic period may be defined as the first three months of gestation. This is the period of major organogenesis. [Shepared, 1980].

The teratogenic drugs are classified into the following categories :-

1. DRUGS PROVED TO HAVE A TERATOGENIC EFFECT AND THIS

INCLUDE :

1.1. THALIDOMIDE : [Fig. I]

In late 1950 a new sedative drug, thalidomide, became available in many countries [Stevenson 1977]. In, 1959 Lenz from West Germany, reported on the occurrence of certain malformations in infants from mothers who had



Fig. 1 Phocomelia. This child was born before thalidomide was available but shows abnormalities associated with its use. More than 6000 malformed babies were associated with its use. Like many drugs, thalidomide had many synonyms and was included in a number of combinations with other drugs.

[Shepared, 1980]

taken thalidomide early in their pregnancy. In a survey on 300 Cases the followings were affected :

arms	152 Cases
arms and legs	80 Cases
arms, legs and ears	9 Cases
arms and ears	17 Cases
ears	21 Cases
legs	5 Cases
Internal organs	5 Cases

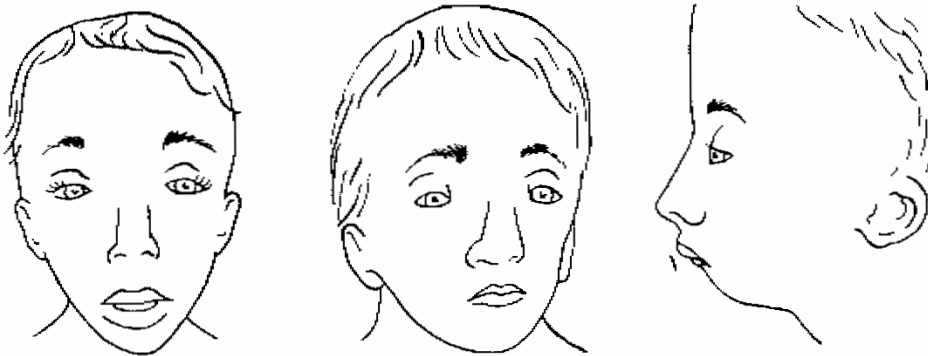
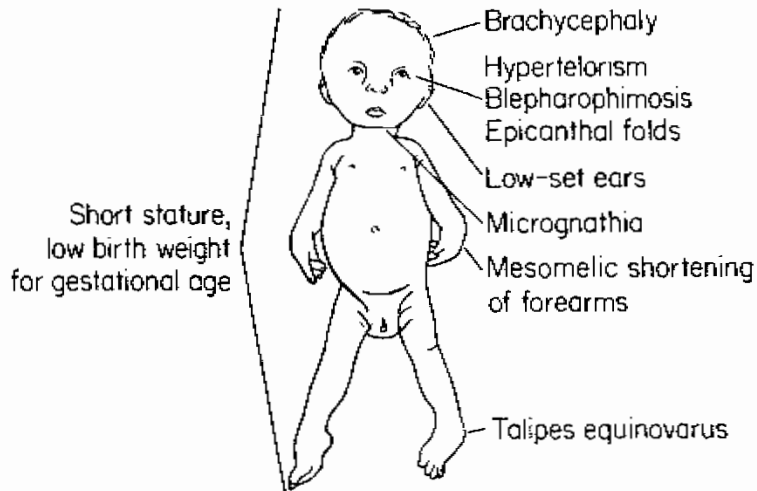
The malformations of limbs were amelia, hemielia, phocomelia, acheria [absent hand], apodia [absent foot], polydactyly, aplasia of radii, aplasia of tibia or femora.

The most frequent malformations in internal organs were : Cardiac anomalies, stenosis or atresia of duodenum or anus, aplasia of gall bladder and anomalies in lungs, kidneys and lower urinary tract. [Stevenson, 1977].

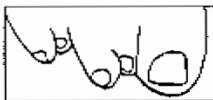
1.2. FOLIC ACID ANTAGONISTS : [Fig.2,3],

Aminopterin and its methyl derivative methotrexate have long been implicated as foetal teratogens , producing a classic clinical picture characterized by growth retardation and malformations of the skull, face

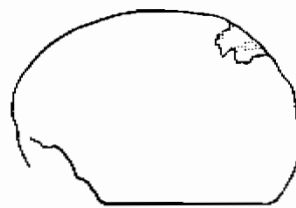
Anti-Folic Acid Embryopathy



Shallow supraorbital ridges, sparse eyebrows laterally, blepharophimosis, prominent nose, low-set ears, micrognathia



Syndactyly, brachydactyly, clinodactyly, enlarged finger joints



Parietal skull defect

Fig. [2] [Goodman and Gorlin 1983]