

VITAMIN-K STATUS BEYOND THE NEONATAL
PERIOD, A PROSPECTIVE STUDY IN NORMAL
BREAST-FED AND FORMULA-FED INFANTS

THESIS

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PRESENTED BY

AMEL AHMED ELINA

M.B., B.Ch.

SUPERVISED BY

PROF. DR. FOUAD EL-BADRAWAY

*Professor of Pediatrics
Faculty of Medicine
Ain Shams University*

PROF. DR. TARIF HAMZA SALAAM

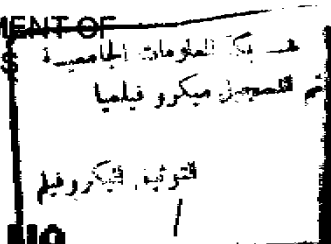
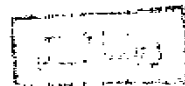
*Professor of Clinical Pathology
Faculty of Medicine
Ain Shams University*

PROF. DR. MOHAMED FARID

*Professor of Pediatrics
Faculty of Medicine
Ain shams University*

**FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY**

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CONTENTS

	Page
INTRODUCTION	1
AIM OF THE WORK	3
REVIEW OF LITERATURE	4
Historical review	4
Sources of vitamin K in infancy	7
Biologic function of vitamin K	11
Vitamin K-dependent clotting factors (Phys- iological implication)	14
Assays of vitamin K-deficiency	20
Clinical manifestations of vitamin K-defi- ciency	24
Treatment of vitamin K-deficiency	36
Vitamin K-prophylaxis	38
Role of vitamin K in haemostasis	42
Blood coagulation mechanism	44
SUBJECTS AND METHODS	49
RESULTS	63
DISCUSSION	83
SUMMARY AND RECOMMENDATION	93
REFERENCES	96
ARABIC SUMMARY .	

INTRODUCTION

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Hemorrhagic disease of the newborn is a self limited bleeding disorder resulting from a deficiency of the coagulation factors depending upon vitamin K namely factor II (prothrombin), VII, IX and X (*Shapiro et al., 1986*). The levels of these factors are about 50% of normal adult value in umbilical cord blood and decline rapidly to reach nadir at 48-72 hours of life (*Sann et al., 1985*). In 0.25-0.5% of infants the decline is so extreme that severe hemorrhage may result (*McDonald et al., 1984*). Thereafter, the levels of these factors slowly increase due to vitamin K absorption from the diet. Vitamin K is approximately four times more concentrated in cow milk than in breast milk (*John and William, 1982*). That is why breast feeding has been implicated as a necessary factor in the pathogenesis of hemorrhagic disease of the newborn infants unless vitamin K prophylaxis is given (*Cornelissen et al., 1992*). Deficiency of vitamin K-dependent clotting factors with

Introduction

clinical bleeding has occasionally been reported in the breast fed infants beyond the neonatal period (*Hogenbirk et al., 1993*).

AIM OF THE WORK

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The aim of this work is to determine whether the type of feeding, breast or formula fed, beyond the neonatal period is associated with changes in the level of vitamin K-dependent clotting factors.

REVIEW OF LITERATURE

HISTORICAL REVIEW

The term hemorrhagic disease of the newborn was first used in 1894 when *Townsend* reported 50 infants with bleeding during the first two weeks of life. The hemorrhage usually began on the second or third day of life and most commonly was from gastrointestinal tract. The observation that this disorder was self-limiting led *Townsend* to differentiate acquired hemorrhagic disease from inherited hemophilia.

Vitamin K was not discovered until 1929 when *Dam* *Seren* observed bleeding in chickens fed a fat-free diet. Afterward, *Brinkhous et al.*, (1937) documented low prothrombin levels in normal newborn infants. Others demonstrated that these low levels could be elevated by the administration of vitamin K (*Waddell and Guerry*, 1939). Hemorrhagic disease caused by vitamin K deficiency was subsequently differentiated from bleeding secondary to other causes; (*Aballi and de Lamerens*, 1962), and the effectiveness of vitamin K administration in the preven-

tion of vitamin K deficiency bleeding was established by *Wefring* in 1962.

Banchet et al., (1966) and *Goldman and Desposito* (1966) described a "new" bleeding syndrome in infants from the age of two months up to one year.

Several publications have appeared presenting the syndrome under a variety of descriptive terms such as "hemorrhagic" diathesis in children associated with vitamin K-deficiency (*Taj-Eldin et al.*, 1966), "hemorrhagic syndrome of early childhood" (*Loveric and Jones.*, 1967), "Vitamin K-deficiency in infants beyond the neonatal period" (*Nammacher et al.*, 1970).

The syndrome has been well established as a vitamin K-deficiency and the administration of vitamin K has a dramatic effect with restoration to normal of vitamin K-dependent clotting factors (*Lizuka et al.*, 1975).

Most striking in the clinical picture is the prevalence of intracranial bleeding which occurs in about

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60% of all cases. This is in sharp contrast to the bleeding syndrome of newborn which occurs on the 2nd to 5th day of life and is dominated by hematemesis or gastrointestinal bleedings (melena neonatorum). The reason for this different predilection of bleeding sites remains a mystery (Chaou et al., 1984).

SOURCES OF VITAMIN K IN INFANTS

The human neonate is not endowed with a surplus of vitamin K, and some are vitamin K deficient at birth (*Shapiro et al., 1986*). This precarious vitamin K status may be the result of a placental gradient for vitamin K. Using high-performance liquid chromatography, *Shearer et al., (1982)* found that vitamin K was undetectable in the cord blood of nine term infants despite levels of 0.13 to 0.29 ng/ml in their mothers. Six additional mothers received vitamin K intravenously prior to delivery, which raised their vitamin K concentration to between 45 and 93 ng/ml. The values found in the cord blood of their infants ranged from undetectable to only 0.14 ng/ml.

The diet is an important source of vitamin K immediately after birth. It is appreciated that early supplemental feeding could reduce the incidence of hemorrhage during the first week of life (*Widder Shoven et al, 1988*).