#### ANAESTHESIA AND BREAST FEEDING

## ESSAY SUBMITTED FOR PARTIAL FULFILMENT OF MASTER DEGREE IN ANAESTHESIA

611-969

SHERIF SAYED ALI SULTAN

M.B., B.Ch.

Supervised By



PROFESSOR OF ANAESTHESIA
FACULTY OF MEDICINE, AIN SHAMS UNIVERSITY



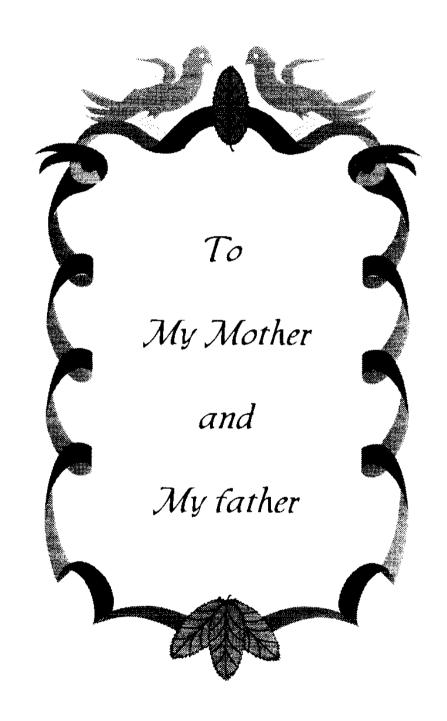
**ASSISTANT PROFESSOR OF ANAESTHESIA**FACULTY OF MEDICINE, AIN SHAMS UNIVERSITY

57931

#### Dr. RAAFAT ABDEL-AZIM HAMMAD

LECTURER OF ANAESTHESIA
FACULTY OF MEDICINE, AIN SHAMS UNIVERSITY

FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY
1994





## lowledgment

anks are all to **God** for blessing me this work until ed its end, as a little part of his generous help life.

I would like to express my deepest gratitude as I am deeply indebted to my professor and supervisor **Prof. Dr. farouk Sadek**, Professor of Anesthesia, Ain Shams University, for his kind moral support, enthusiastic encouragement and help to pursue this effort.

Also, I am particularly very grateful to **Prof. Dr. Amir Salah**, Assistant Proffessor, Ain Shams University, for his great support, really, it is a great honour to work under his guidance and supervision.

I would also like to express my very sincere thanks to Dr. Raafat Abdel-Azim, Lecturer of Anethesia, Ain shams University, for his great support, patience and the tremendous effort he has done in the meticulous revision of the whole work.

No words can describe my heartiest gratitude to all staff members and my colleagues in Anaesthesia Department for their continuous support and help.

Finally, I sincerely hope that this work achieve something in our work in anaesthesia.

Sherif sayed Sultan

#### CONTENTS

Topic		Page
Introductio	on.	1
Chapter 1		2 - 10
	- Advantages of human breast milk	7
Chapter 2		11 - 26
	<ul> <li>Maternal pharmacokinetics</li> </ul>	11
	<ul> <li>Mammary pharmacokinetics</li> </ul>	12
	- Infant pharmacokinetics	22
	<ul> <li>General guidlines in drug use during breast feeding</li> </ul>	24
Chapter 3	The effect of Anaesthesia on Breast feeding	27 – 69
	<ul> <li>Drugs interfering with milk production</li> </ul>	28
	- Drugs affecting the suckling infants	28
	- Opioids	29
	<ul> <li>Non-opioid analgesics</li> </ul>	38
	<ul> <li>Intravenous induction agents</li> </ul>	41
	<ul> <li>Inhalational anaesthetic agents</li> </ul>	43
	<ul> <li>Neuromuscular blocking agents</li> </ul>	45
	- Anticholinergics	46
	- Anticholinesterases	47
	- Local anaesthetic agents	48
	- Benzodiazepines	50
	- Antibiotics	54
	- Histamine H, receptor antagonists	58
	- Antiemetic and neuroleptic drugs	5.8

	-	Anticoagulants		59
	~	Cardiovascular drugs		60
	<b>-</b>	Drugs used in treatment of bronchialasthma		62
	-	CNS stimulants		62
	-	Drugs used in obstetrics		63
	-	Antidiabetics		63
Sur	mmary		70	- 71
Re	ferences		73	- 102
Ara	abic Summary			

#### List of Figures

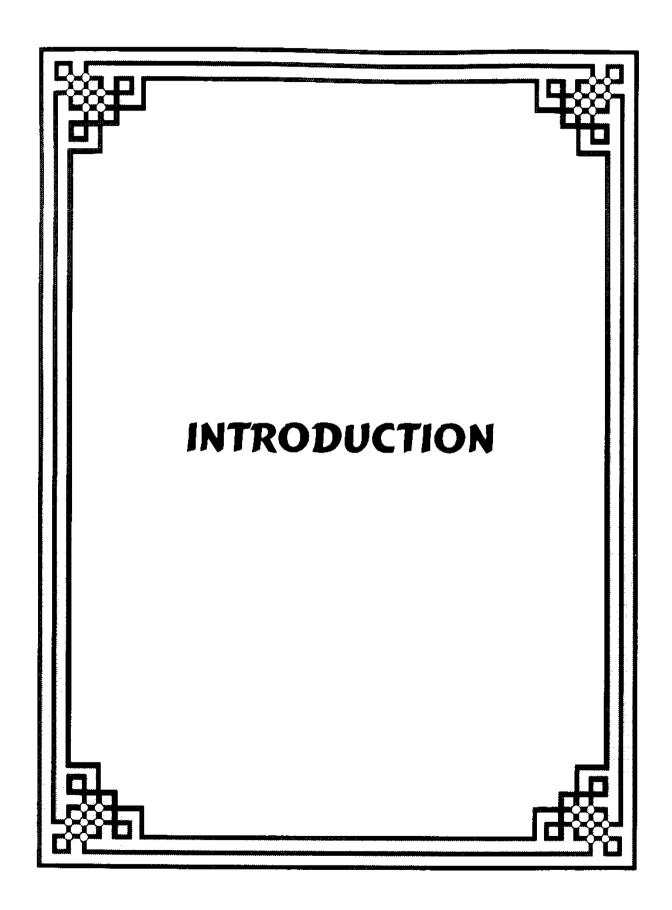
Figure No.	Description	Page
Fig. 1	Changes in rates of secretion of oestrogen, progesterone, and prolactin for 8 weeks prior to parturition and for 36 weeks thereafter.	4
Fig. 2	Excretion of antipyrine in human milk & saliva.	19
Fig. 3	Fentanyl concentration in colostrum and serum.	35

#### List of Tables

Table No.	Description		
Table 1	Approximate composition of colostrum and mature milk.	7	
Table 2	Percentage of maternal drugs appear in milk	20	
Table 3	Physical-chemical properties of some opioids	30	
Table 4	Pharmacokinetic properties of some opioids	30	
Table 5	Elimination half-lifes of some opioids in adults and neonates	31	
Table 6	Differences in pharmacokinetics of morphine between adults and neonates	32	
Table 7	Relative and absolute daily dose in milk of some opioids	33	
Table 8	Half-lives of some intravenous anaesthetics in adults and neonates	43	
Table 9	Elimination half-lives of local anaesthetics in adults and neonates	50	

#### List of Tables

•	Table	No.	Description	Page
	Table	10	Elimination half-lives of some benzodiazepines in adults and neonates	51
	Table	11	Relative and absolute daily dose in milk of some benzodiazepines	51
	Table	12	First skin contact with the infant after caesarean section	67
	Table	13	Breast feeding frequency after caesarean section	67

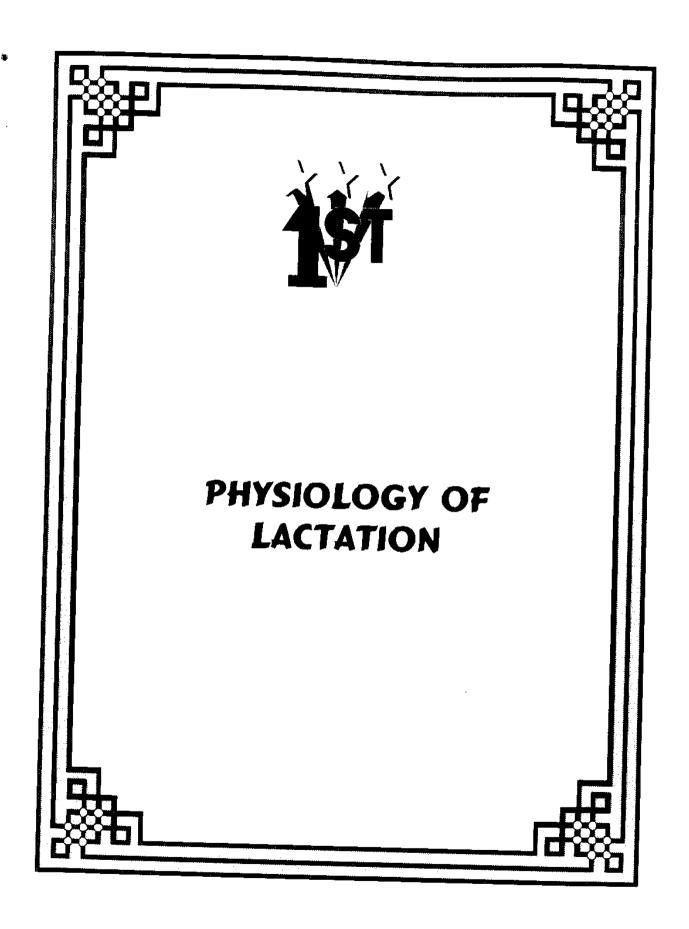


### Introduction

It is common for anaesthesiologists to encounter nursing mothers who invariably question whether breast feeding after anaesthesia can harm their infants. It is also a question between anaesthesiologists "What is currently the best method of anaesthetizing a breast feeding mother so that her infant is not subjected to harmful effects of anaesthetic agents transmitted in breast milk". Anaesthesiologists searching for information on the excretion of anaesthetic drugs in breast milk, and their potential hazards to suckling infants are often unsuccessful in finding it in the standard anaesthetic textbooks. They only find limited data on clinical experience in the literature with little relevance to the anaesthesiologists, (Bond and Holloway, 1992).

Medical professionals too often simply discourage breast feeding when giving a drug that is known to pass into breast milk, turning to artificial feeding. Breast feeding has immunologic benefits, nutritional superiority, economic, and psychological advantages which are mostly deficient in artificial feeding. There are only few absolute contraindications to breast feeding, anaesthesia and surgery should not be one of them. Breast feeding should be encouraged and not interrupted by every mean, (Cunningham et al, 1991).

Anaesthesiologists require a good knowledge of the excretion of drugs in breast milk and the potential hazards to suckling infants of drugs ingested via breast milk.



# Physiology of Lactation

#### Development and Anatomy of the Breast

Development of the mammary gland begins at about 8 weeks of foetal life, (Neville, 1983). In the third trimester high concentrations of foetal prolactin stimulate terminal differentiation of ductal cells into two concentric layers of cuboidal cells and a central lumen. The inner layer of cells gives rise to the secretory epithelium, while the outer layer becomes myoepithelium. Milk secretion by the infant following delivery is not uncommon, (Pritchard et al, 1989). The human is the only animal in which significant growth of the mammary gland occurs in the absence of pregnancy, at puberty, (Glasier and McNeilly, 1990).

The basic glandular secretory units of the breast are the alveoli which cluster around ductules forming 15-20 lobes for each mammary gland.

#### Changes in Pregnancy

In the first trimester ductal system hyperplasia occurs, also with rapid increase of alveolar number under the effect of the tremendous amounts of oestrogens secreted by the placenta. In the later pregnancy, alveolar cell hypertrophy, preparing the breasts to be milk-secreting organs, occurs under the effect of progesterone. Other hormones, namely, growth hormone, prolactin,

the adrenal glucocorticoids, and insulin are needed for development of breasts during pregnancy, (Yoshinaga, 1987).

#### Initiation of Lactation Function of Prolactin

Lactogenesis is triggered by a fall in progesterone concentrations in the presence of mammary development and prolactin concentrations sufficient to allow milk secretion (Fig. 1). After delivery of placenta, progesterone and oestrogen fall over 5-6 days and prolactin over 14-21 days unless suckling occurs, (Glasier et al, 1984).

Prolactin is necessary for the onset and continuation of lactation, and this is demonstrated by the fact that a specific dopamine agonist such as bromocriptine inhibits prolactin secretion and prevents milk production, (Ylikorkala et al, 1982).

Prolactin is secreted by the mother's pituitary gland and its concentration in her blood rises steadily from the fifth week of pregnancy until birth of the baby, usually about 10 times the normal non pregnant level. In addition, the placenta secretes large quantities of human chorionic somatomammotropine which also has mild lactogenic properties. Even so, only a few milliliters of fluid are secreted each day before delivery. Oestrogen and progest one inhibit the lactogenic influence of prolactin on the mammary gland, (Bennett et al, 1988).

Mechanisms underlying the release of prolactin during suckling are poorly understood, but it is suggested that suckling at the nipples may result in changes in dopamine turnover, allowing prolactin to be released into the circulation. The changes in dopamine turnover may be secondary to suckling-induced

increase in opioids such as  $\beta$ -endorphin which may also influence release of gonadotropin releasing hormone (GnRH), (Gordon et al, 1987). There has been a report of increases in plasma  $\beta$ -endorphin concentrations during suckling in women but a direct relationship has yet to be confirmed, (Franceschini et al, 1989).

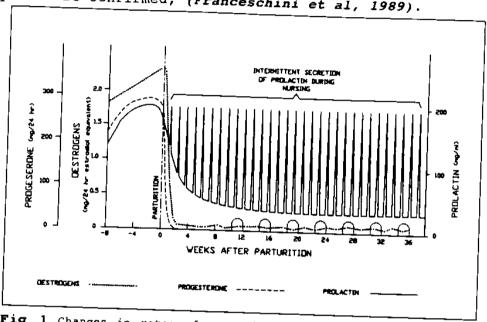


Fig 1 Changes in rates of secretion of oestrogen, progesterone, and prolactin for 8 weeks prior to parturition and for 36 weeks thereafter. It is to be noted that prolactin secretion get back to basal levels within a few weeks with intermittent periods of marked prolactin secretion for about one hour during and after periods of nursing, (Guyton, 1991).

The secretion of milk requires an adequate background secretion of most of the mother's other hormones as well, but important of all are growth hormone, the adrenal glucocorticoids and parathyroid hormone. These hormones are necessary to provide the amino acids, fatty acids, glucose and calcium that are required for milk formation. Also, both free and bound levels of thyroxin are reduced and thyroid hormone binding globulin levels are increased during lactation in women although there appears to be no specific role for these hormones in milk production, (Neville, 1990).