CHANGES IN THE CERVICAL FACTOR OF FERTILITY WITH INTRA UTERINE DEVICE

THESIS

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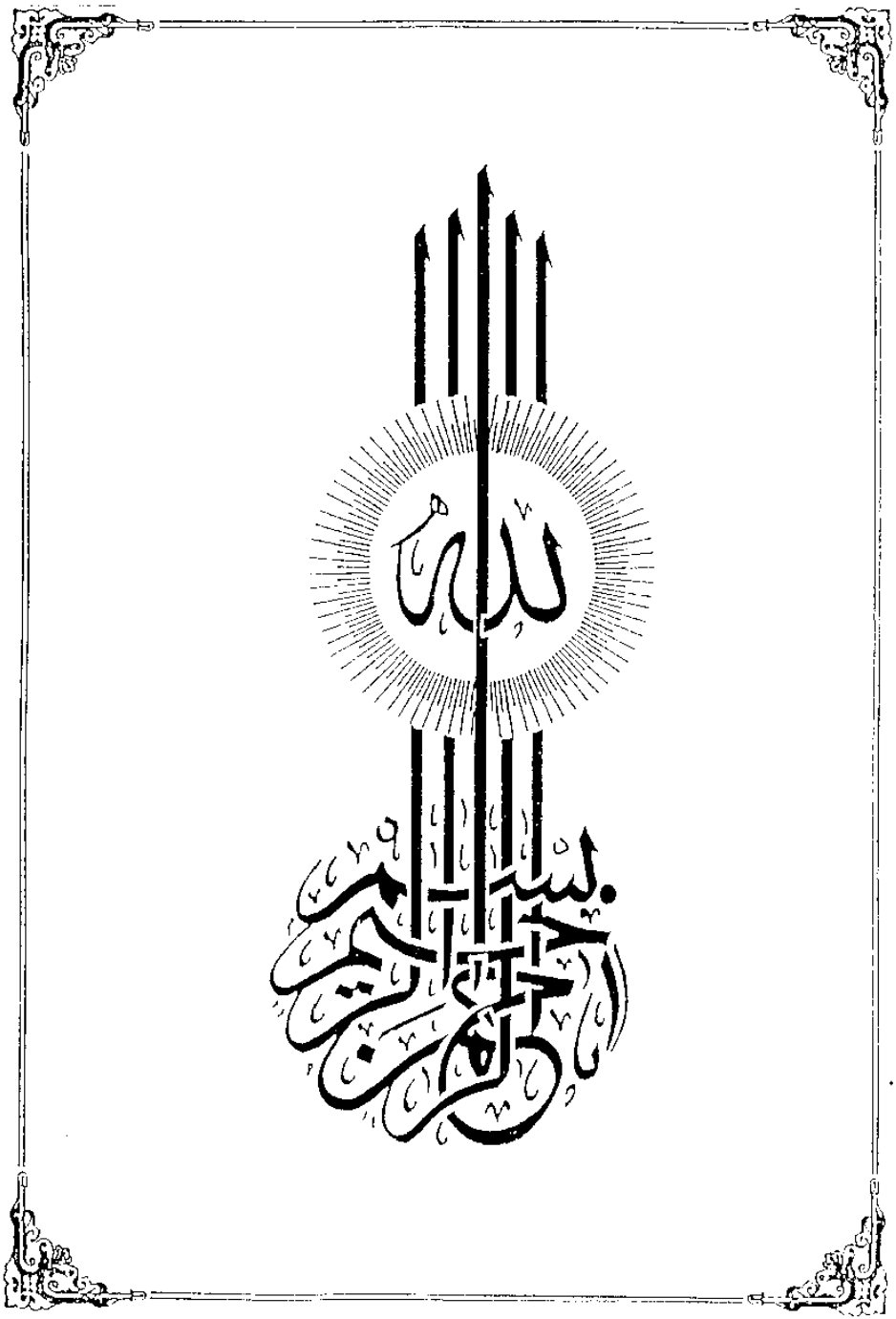

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C O N T E N T S

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INTRODUCTION

I N T R O D U C T I O N

For centuries use has been made of some sort of intra-uterine device in order to prevent pregnancy . Although the effect of the modern IUD is considered to be less than the present day oral contraceptive , it has the advantage of not requiring daily attension . The use of the IUD has increased more rapidly during the past decade than the use of any other contraceptive method and has now become a major method of contraception in family plannig programmes in many parts of the world (Van Os , 1983)

The device most commonly used a decade ago was lippes loop but its clinical performance was not entirely satisfactory . Within two years 10.8 per cent were expelled spontaneously , 16.2 per cent were removed on account of bleeding , pain or both, 3.8 per cent of women became pregnant with the device in situ or following an unnoticed expulsion (Tietze and Lewit , 1970) . Moreover , excessive uterine bleeding is a serious problem specially in developing countries where the incidence of anaemia is high (Hefnawi , et al. , 1975) . Therefore a search continued for newer devices which lowered the expulsion rate , prevented bleeding disturbances and decreased the incidence of pregnancy (Hefnawi ; 1979) .

The copper IUD is less often spontaneously expelled from

the uterus , produces fewer cases of irrigular bleeding and causes less pain than the non-medicated bulky linear-shaped devices (Zipper , et al. , 1971) . But still the occurrence of pregnancy with intra uterine device is a major drawback to their use as a conteaceptive technique . A recent study using a highly sensitive assay for beta subunit of human chorionic gonadotrophin concludes that the copper device interferes with implantation and establishment of pregnancy but not with fertilization and blastocyst formation (Rowe , 1977) . Yet it is not clear how the intra-uterine environment turns hostile to the formed blastocyst , preventing its implantation or further development . Thus , little is known about the precise infertility mechanisms beyond the fact that it is local rather than systemic (Hefnawi , 1979) .

Aim of the study

The purpose of this study is to access the possible changes which may occur in the cervical mucus that may alter sperm transport through the cervix after application of copper IUD.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Cervical mucus :

Cervical mucus that accumulates in the vaginal pool may contain endometrial , oviductal , follicular , and peritoneal fluids as well as leucocytes and cellular debris from the uterine , cervical and vaginal epithelia . The endocervical crypts in women of reproductive age secrete 20 - 60 mg of mucus per day ; the level of secretion increases to 700 mg per day during mid cycle (Odeblad , 1966) . Once secreted by the cervical crypts , which are at right angles to the cervical canal , cervical mucus is released perpendicularly to the axis of that channel . Probably as a result of the force of gravity, the filaments flow down parallel to the axis . The cervical canal thus acts as a capillary tube where the main filaments have a parallel arrangement . Once the column of cervical mucus flows out of the external os , it is suspended within the vaginal fluid , accumulating in the vaginal fornix . There cervieal mucus is freed of the capillary biophysical constraints encountered in the canal . After intercourse , spermatozoa enter into the cervical mucus , where they are protected from the acidic pH of the vaginal millieu and are transported rapidly between the micelles of the mucus within the vaginal pool .

Cervical mucus is rheologically heterogenous , reflecting compositional differences in situ (Hafez , 1980) . The nature of the secretion varies in different sites so that cervical mucus is never a homogenous material but a blend of elements which have formed as mucoid globules within each tall columnar cell which lines the glands , and leaves their surface to join the main mucous stream .

Regulation of cervical mucus secretion :

Mucus secretion is a continuous process throughout each cycle, with its amount and consistency primarily under estrogen and progesterone regulation . Post menstrually it is scanty , tacky and cellular and gradually builds up to acheive a peak in amount and clarity at ovulation time under the influence of estrogen secretion . In the post ovulatory phase , progesterone secretion rapidly reverses these changes and daily quantity of mucus secreted is reduced from an ovulatory peak of perhaps 3 ml (Odeblad , 1959) .

Other factors may influence mucus secretion either directly , when measurement of oestrogen levels and output is usually within the normal range and the explanation of unfavourable cervical mucus appears to lie in the inability of the cervical

glands to respond favourably to adequate ovarian stimulation . Local neuromuscular factors may restrict or modify the glandular secretions , or indirectly , when autonomic imbalance related to emotional disturbance contributes to hypothalamic dysfunction which may contribute to anovulation (Philipp and Carruthers , 1981) .

Biochemical composition :

The cyclic changes in mucus properties during the menstrual cycle reflect changes in the concentration and perhaps even in the composition of cervical mucus (Zavos and Cohen , 1980) . Cervical mucus consists of approximately 92 to 95% water .

Inorganic salts in the mucus amount to 1% of which the principal constituent is NaCl . Traces of potassium , magnesium , calcium , copper , phosphates ,sulfates , and bicarbonates are also present (Moghissi , 1980) .

Low molecular weight organic compounds present include free simple sugars (glucose , maltose , mannose) , amino acids , cholesterol,lipids , ascorbic acid , and polysaccharides (Hafez, 1980) .

High molecular weight compounds include :

- Cervical mucin a carbohydrate rich glycoprotein . It is the most important constituent of cervical mucus , and is markedly increased immediately before or simultaneously with the time of ovulation . Most of the physical and biologic characteristics of cervical secretion are due to the presence of mucin (Moghissi , 1980) .
- Plasma proteins - albumin , globulin , lipoprotein , immunoglobulin .
- Specific proteins - lactoferrin (iron binding protein , bacteriostatic) .
- Enzymes such as alkaline phosphatase , esterase , aminopeptidase , amylase , and certain components of fibrinolytic enzymes (Hafez , 1980) .

Protein constituents :
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Several studies have indicated that albumin , γ-globulin , and $\alpha_1$antitrypsin , along with a number of other proteins , are present in cervical mucus throughout the menstrual cycle and are decreased at ovulation time .(Moghissi , 1980) .

Lactoferrin , an iron binding protein , is among the several proteins of cervical mucus that are absent or poorly presented

in blood plasma . Its secretion may reach 1 mg/ml , lactoferrin with bacteriostatic activity , is synthetizd by other types of tissues :

1- The acini of glandular epithelia , such as those from bronchial mucosa , salivary , or mammary glands .
2- The kidney tubules , and
3- Those myeloid cells that are the precursors of neutrophilic leukocytes .

All soluble proteins in cervical mucus reach their minimal concentration around the time of ovulation . The copious flow (mucorrhea) coinciding with ovulation prevents accumulation of proteins transudating from plasma or released by leukocytes, whereas the decrease in mucus flow due to progestogens favours enrichment of mucus in substances that have access to cervical crypts (Hafez , 1980) .

Structural and chemical nature of cervical mucus :

Although , there are considerable changes in the amount and physical nature of the cervical mucus at different stages of the cycle , they are related almost entirely to water content and molecular arrangement with little change in the other chemical constituents .

In general terms cervical mucus is a hydrogel , the gel component consisting of long thread-like , flexible mucoid molecules suspended in a liquid phase . The liquid phase consists of an aqueous solution of salts and proteins . Albumin and globulins of various types have been separated by electrophoresis , and the overall constitution is similar to plasma (without fibrinogen) diluted with physiological saline .

The changes that occur in the mucus during the various phases of the cycle are almost entirely related to the molecular alignment , and the aqueous phase that is retained between them .

The exact chemical composition of the mucoid element has not been agreed , but is probably a glycoprotein with neutral alkaline and acid mucopolysaccharide elements , and the total concentration of such solids ranges from 2% at mid cycle to 12% at the maximal luteal phase . The crystalloid contents of the aqueous phase are in physiological concentration similar to Ringer solution .

Other substances are disolved in it , including the serum proteins , and globulin derived from the mucous epithelium .ABO blood iso- agglutinins have been identified in the mucus , Alkaline phosphatase appears related to estrogen secretion . Some free sugars (including glucose) and amino acids are present ,