CYTOLOGIC FINDINGS IN THE ENDOMETRIUM OF INTRAUTERINE CONTRACEPTIVE DEVICE USERS, THEIR RELATIONS TO THE ENDOMETRIAL HISTOLOGY

THESIS

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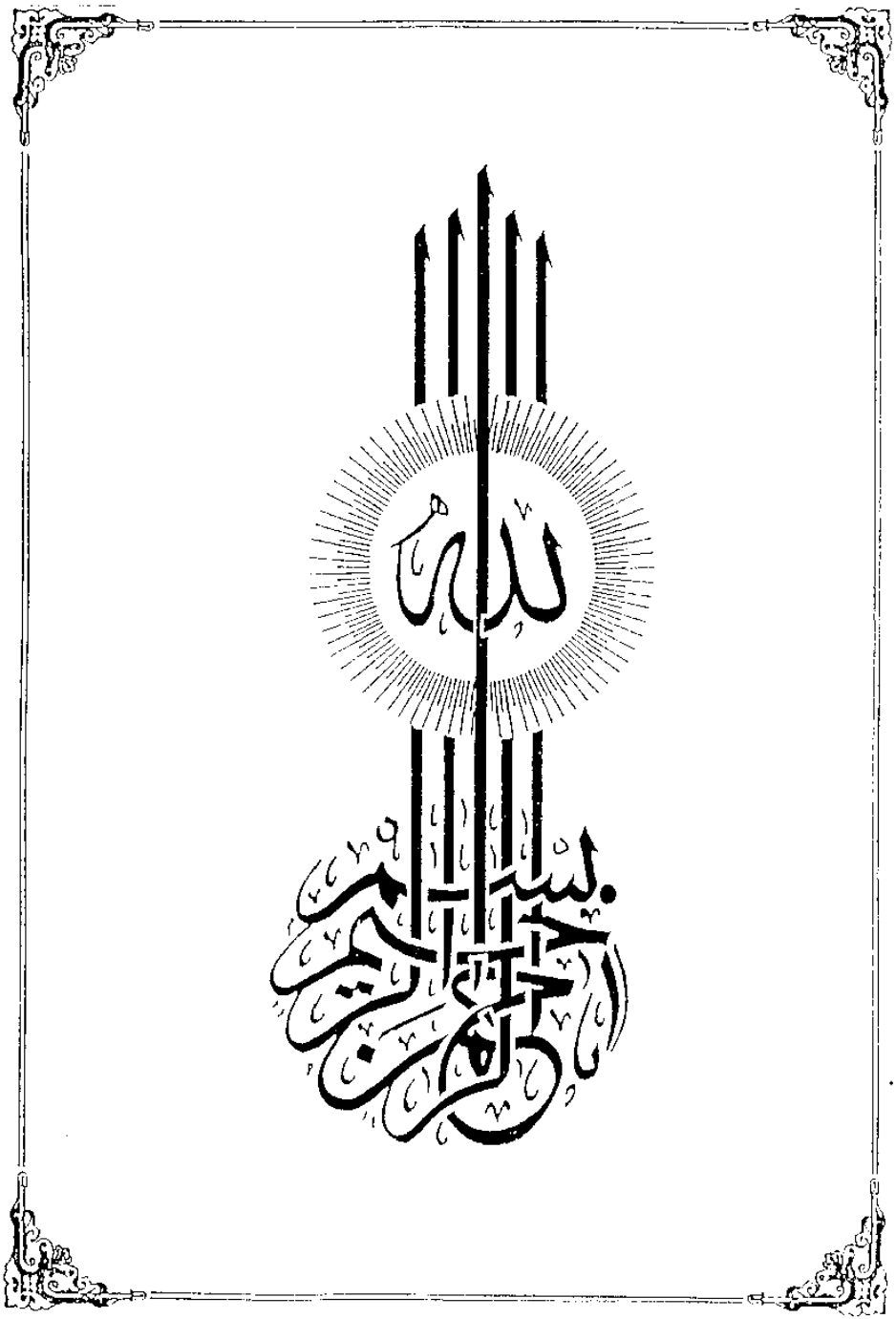

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INTRODUCTION

Control of population continues to be one of Egypt's major national concerns.

Among the several permaneht and reversible means of contraception, intrauterine contraceptive devices (IUDs) have for many years played an important role in the effort to limit population growth (Nayar et al 1985). Encouraging results have been reported from several countries, besides the reliability and inexpensiveness of the recent IUD render it a valuable method in global population control (Haukkamaa et al 1986).

Unfortunately, sepsis is one of the major complications caused by prolonged usage of an IUD (Liskin and Fox 1982). Together with vaginal bleeding and pain, are the main medical reasons for women to discontinue using IUD. (El Makhzangy et al 1983)

Studies carried out in western countries have noted an association of actinomycosis with IUD usage espicially plastic types (Duguid et al 1960) and (Sykes and Shelly 1981). Such complication associated with certain types of IUD and certain organisms reinforce the idea that the IUD plays a direct role in both inflammatory and infectious diseases (Schmidt 1982)

Again, while an increasing number of women are currently being fitted with IUDs, doubt exists to their mode of action and their long term effects (Bogaert 1983)

Of particular interest is the question as to whether prolonged retention of foreign body like an IUD in the uterus may have a local carcinogenic action or not (Castadot et al 1980).

AIM OF THE WORK

The aim of this work is to study the cytological and histopathological features of the endometria of those women using intrauterine contraceptive devices (IUD) for variable periods of time, in order to evaluate their short and long term effects on the endometrium.

The cytological findings will be compared with the histopathologic changes in order to assess the value of endometrial cellular sampling technique in detection of various endometrial lesions without anaesthesia.

In the course of the present study a trial will be carried to answer some enquiries connected with the use of IUD as a good method of contraception e.g:

1) Is there a relation between IUD use and the reported increasing incidence of upper and lower genital tract infection and neoplasia.

2) The possible role of cytology for follow up of women using IUD.

REVIEW OF LITERATURE

CHAPTER I INTRAUTERINE CONTRACEPTIVE DEVICES

IUD

A - Ovarian Function with IUDs

Hansel and Wagner (1961) in their experimental study with cattle reported inhibition of the corpus luteum with shortening of the estrus cycle after the insertion of a foreign body into the uterine cavity.

Vorys et al (1964) measured the FSH and the LH of the anterior pituitary in 3 women using the IUDs and concluded that the device might alter the phase of the corpus luteum.

Sammour et al (1967) pointed strongly in their study to the possibility that the mode of action of the IUD in preventing pregnancy may be through hormonal changes in the body. They observed decreased estrogen level in the first half of the cycle as proved by the pyknotic index curve, as well as early degeneration of the corpus luteum with shortening of the secretory phase as proved by histologic examination of the endometrium.

On the other hand, Fotim et al (1967) demonstrated that ovarian function is unaffected by the presence of an IUD.

Ishikawa et al (1971) said that as far as cytologic examinations are concerned, the presence of an IUD does not have any effect on the menstrual cycle or ovarian function of women.

B - MODE OF ACTION OF IUDs

The mechanism of which intrauterine devices prevent conception in human has not been established.

Margulies (1960) suggested that IUD interfere with ovum and/or spermatozoa transport by producing alterations in uterine and tubal motility.

Mastrianni and Hongsanand (1964) supported this concept in their study on Rhesus monkey.

However, Morgenstern et al (1966) observed in their study that IUDs does not prevent transport of sperms to the site of fertilization.

Davis (1972 suggested that macrophages induced inflammatory reaction may phagocytoze spermatozoa or ova.

Hsu et al (1976) suggested a direct spermatocidal action of IUDs.

Jessen et al (1963) have theorized that the IUD might alter the endometrium in some manner which disturbs implantation.

Bonney et al (1966) Tammada et al (1967) and Lallenbach - Hellweg (1961) put more emphasis on the alteration in the hormonal synchrony. They reported that the IUD has the effect of altering the synchrony of the endometrial maturation, so that the endometrium is out of phase with the ovum when it reaches the endometrial cavity.

According to Parr (1983) the influx of intrauterine inflammatory cells after IUD insertion create a uterine milieu which is hostile to the unimplanted embryo and possibly to sperm as well.

This concept was also supported by Moyer and Mishell (1971).

Sagiroglu and sagiroglu (1970) thought that macrophages play a major role in insuring contraception. Its products such as proteases and prostaglandins are also incorporated (Myatt et al 1975).

Cassien and Ohlsson (1981 observed that serum proteinase inhibitors concentration in uterine fluid is low in the proliferative phase and at mid cycle (time of ovulation).

Measuring these levels in IUD users, they found the reverse, there is increased concentrations in this time. They noted that this may result from an increased transudation associated with local inflammation of the endometrium with IUDs. They suggested that this increased amounts of inhibitors may disturb intrauterine stages of reproduction.

Grasso et al 1983) estimated small amounts of interferon released in the uterine fluid of IUD users. They suggested that interferon with its known antiproliferative and antidifferentiation effects could play a contraceptive role.

On the other hand, Hansel and Wagner 1980), Worys et al (1964) and Sammour et al (1987) pointed strongly to the possibility of hormonal changes in the

body caused by IUDs. They suggested corpus luteum alterations.

Hobub et al (1971) suggested an immunological basis for the contraceptive effect of IUDs.

Hatcher et al (1984) summarized the following possible mechanisms :

1- Local foreign body inflammatory reaction causing lysis of the blastocyst and sperm, and/ or prevention of implantation.

2- Increased local production of prostaglandins which inhibit implantation.

3- Competition of copper and zinc, inhibiting carbonic anhydrase and possible alkaline phosphatase activity. Copper may also interfere with estrogen uptake and its intracellular effects on the endometrium.

4- Disruption of proliferative - secretory maturation process by progestin producing IUDs.

5- Disruption of implanted blastocyst from the endometrium by mechanical effect.

6- Increased motility of ovum in fallopian tube.

7- Immobilization of sperms as they pass through the uterine cavity.

C - IUD ALTERATIONS

According to Gupta et al (1971) degenerative changes occur on the surface of both inert plastic and ou-tiated IUDs. The surface of a new IUD is smooth, glistening and uniform. An IUD that has been in the uterine cavity for 6 months or longer reveals changes that can be seen microscopically and sometimes grossly. These changes are progressive. An IUD that has been in situ for 36 months or longer may reveal obvious, gross disintegration. The surface of the IUD, instead of being smooth and glistening becomes irregular and cobblestoned with large irregular calcium, iron and protein compound deposits.

Luff et al (1978) observed fragments of IUD substance in the Fallopian tubes.

Frost (1979) described that the disintegration of the IUD and its encrustation with calcium and iron compounds can sometimes be detected cytologically in Pap smears (cervico-vaginal Pap smears). It is represented by non refractile, coated plastic or metal fragments seen as flakes of 50 um to 200 um which are brown or brownish black with dense centres. These flakes are usually surrounded with acute and chronic inflammatory cells. Occasionally a foreign body giant cell reaction with histocytic proliferation may be observed. These fragments are called IUD associated material.

Using the scanning electron microscope Schmidt et al (1980) revealed a variety of cellular, organic and inorganic materials that give rise to a complex surface coating not only on the IUD but on the tail as well.

This surface coat is frequently described as 'adherent material' by many workers.

According to Sheppard and Bonnar (1980) the organic surface-coat is composed of mucoid and cellular elements. The cellular elements have been shown by electron microscopy to consist of macrophages, PNL, platelets and fibrin. In some cases a definite pattern of fibrinoid deposits, intact cells, cellular debris and crystalline structures is seen.

Josden et al (1977) and Sheppard and Bonnar (1980) demonstrated varying amounts of calcium deposition in the inorganic component of adherent material on the surface of IUDs. The detailed nature of this coating remains undescribed.

Schmidt (1982) stated that through mechanism that are not thoroughly understood but that collectively be considered surface ulterations, the IUD becomes increasingly recognized as a foreigner to the host. Furthermore, the altered IUD is associated with and may even be the cause of an increased inflammatory response as time passes. He said that the altered IUD may become a host to pathogenic organisms thus may contribute to the development of serious PID. He called attention to the importance of duration of the IUD inside the uterine cavity, and the IUD related inflammatory and infectious diseases.

Marrie and Costerton (1983) observed different morphologic types of bacteria adherent to the devices they examined, often buried in a thick biofilm. Electron microprobe analysis revealed the presence of calcium in the biofilm formed by bacterial

colonization. They said that understanding of the mechanism of adherence of bacteria to these devices could lead to the development of a device which will resist bacterial colonization.