# CYTOGENETIC STUDY ON WOMEN USING DEPO-PROVERA

A Thesis

Submitted for partial fulfilment of

MASTER DEGREE

of Obstetrics & Gynecology

by

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To those who gave me the true love and the warmest feelings, to my Father and Mother, asking God to preserve and bless them.

Dr. Nasser El Kholy
Cairo, 1987

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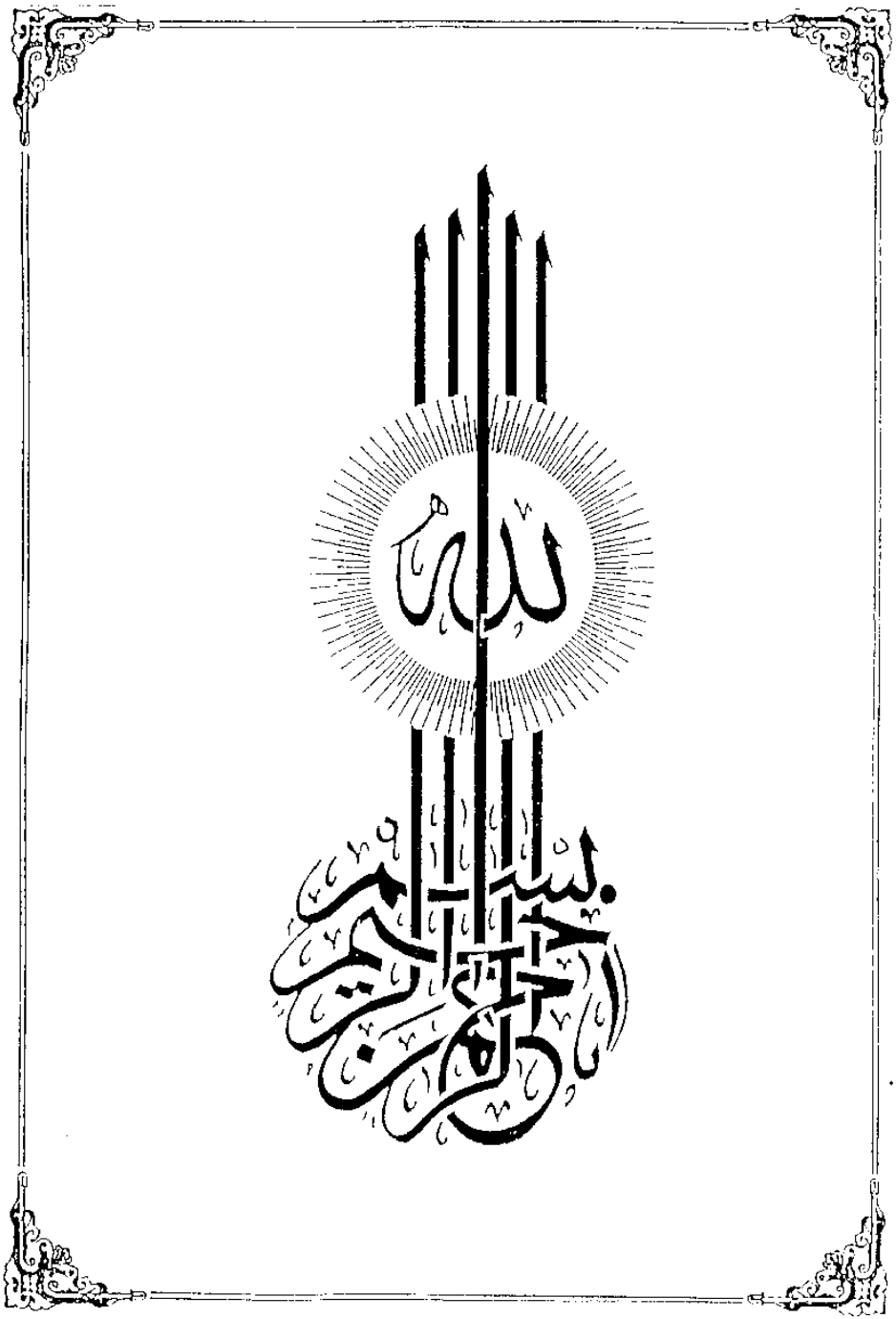


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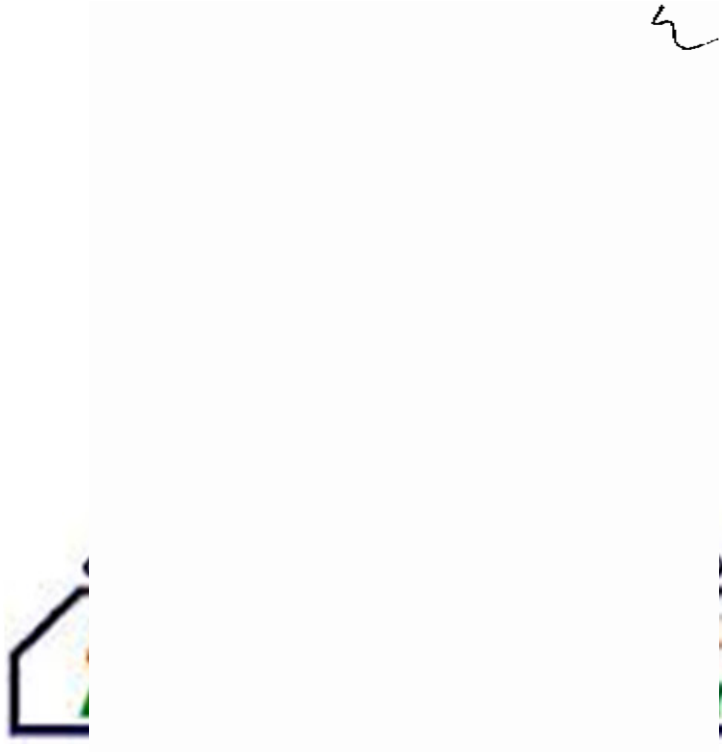

# ACKNOWLEDGEMENT

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## ACKNOWLEDGEMENT

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# INTRODUCTION

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# INTRODUCTION

Hormonal contraceptives are among the most widely used drugs all over the world. The value and efficacy of these compounds in the face of an ever increasing population explosion, cannot be ignored; however, there is no single drug devoid of ill effects and hormonal contraceptives are no exception to this rule.

The potential benefits and side effects of drug, must however, be weighed up against the deleterious effects of the disease itself, even if pregnancy was a "disease" state [particularly, if the physical and psychological risks associated with pregnancy are considered].

The main difference between hormonal contraceptives and other drugs is the possible long term use of hormonal conctraceptives. Some of the adverse effects have already been recognized, some at present are merely suspected and perhaps the potentially most important ones still elude us. In this last category are possible damaging effects on the genetic material.

In spite of the fact that contraceptive steroids have been the subject of more scientific publications than any other drug in history, their effects on chromosomes are scantly documented and controversial (Goh, 1967; Badr et al; 1969, 1971; Fitzgerald et al; 1973; Guttierrez and Lisker, 1973; Matton-Van Leuven et al; 1974 and Pinto, 1986).



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The aim of this study is therefore, to try to elucidate the possibly harmful effects of hormonal contraceptives on the genetic material, using chromosome breakage under controlled conditions as a test system.



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# REVIEW OF LITERATURE

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## REVIEW OF THE CURRENT LITERATURE

Population explosion is considered as one of the most important problems facing most of the developing countries including Egypt.

The population in Egypt is increasing very rapidly at a rate of about 2.3% yearly (Statistical Year Book of Egypt, 1975).

All evidence indicate that the socio-economic problems which resulted from this population explosion could be solved not only by increasing national income but also by decreasing birth rate through family planning programs.

In Egypt, there are 13.4 million women who can give birth every year (Statistical year book of A.R.E. 1975) and hence, it is realized that a family planning program would give us a good chance to reach a large number of highly fertile women.

In general any contraceptive to be ideal should be effective, simple to use, unexpensive, safe, reversible, does not interfere with sexual act and has no immediate or late side effects.

Reports from family planning programs around the world show that when women were offered a choice among contraceptive methods which included an injectable, 25 - 75% of them would choose the injectable (Seymour et al; 1970; Hornsby, 1972;



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Kesseru-Koss et al; 1973; Vechio, 1973; McDaniel, 1974 and Patterson, 1974.

Effectiveness, convenience and freedom from fear of forgetting are the major reasons for popularity of Depo-Provera (Patterson, 1974).

An important advantage is that Depo-Provera does not inhibit lactation as the oestrogen-progesterone oral contraceptives sometimes do (Gomez-Rogers et al; 1967; Zanartu, 1968; Kora, 1969; Karim et al., 1971 and Koetsawang et al., 1972). In fact, Depo-Provera may actually increase both the duration of lactation (Gomez-Rogers et al., 1967 and Guiloff et al., 1974) and the volume of milk (Hefnawi et al., 1970; Karim et al., 1971; Koetsawang et al., 1972 and Hefnawi et al., 1975). It is therefore, preferable to oral contraceptives for postpartum use, especially in countries where mothers breast feed their children for long periods (Hefnawi et al., 1970 and 1975).



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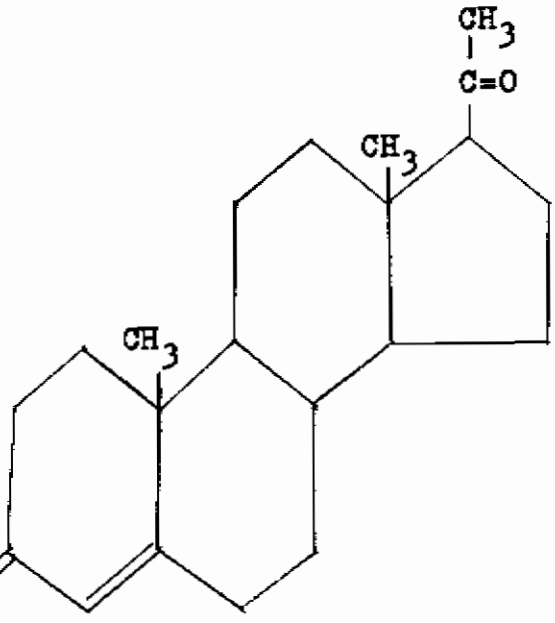
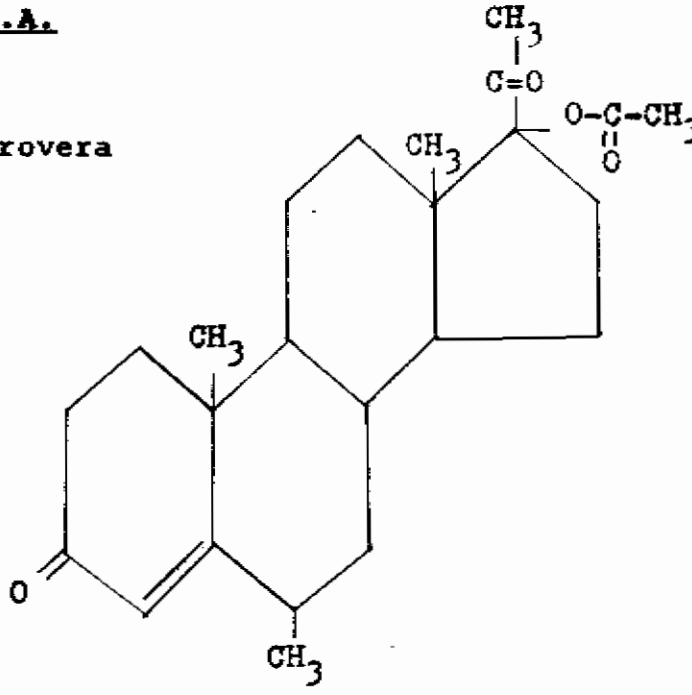
## MEDROXY PROGESTERONE ACETATE

**M.P.A.**

**Depo-Provera**



Progesterone



Medroxyprogesterone Acetate

Medroxyprogesterone acetate (6 α - methyl - 17 α Hydroxyprogesterone acetate) is highly potent, long acting progestational compound. It is white crystalline powder, insoluble in water, soluble in ether and benzene. Its melting point is 203 - 205 °C.

Medroxyprogesterone acetate is 24 - 48 times as potent as progesterone when administered subcutaneously as indicated in the studies done in immature rabbits (Gunning, 1967). It was reported that medroxyprogesterone acetate is devoid of any androgenic (Dorfman, 1948), oestrogenic (Rubin et al., 1951)



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anabolic ( Herchberge et al; 1958) and corticoid (Beatty et al., 1954; Stafford et al.,1958 ; Singer & Barman, 1955) activities.

On the other hand, it has an anti-oestrogenic effect (Edgren & Calhoun, 1959), which is equivalent to that of progesterone.

Unlike progesterone medroxyprogesterone is cleared only slowly from the plasma. The majority is excreted via the bile and some in the urine as glucuronide (Ronald, 1978).

A single depot-injection of 50 mg will sustain a rise in temperature for four to six weeks. There is no change in sodium, potassium or nitrogen balance at a dose of 100 mg daily (Kistner, 1969). There is some adrenocorticoid, some anti-oestrogenic activity and the growth hormone response to hypoglyceamia is reduced.

Virilizing effects have been seen in the female foetus of rats and rabbits and there is a single report of minimal androgenic change in the human foetus (Burstein and Wasserman, 1964).



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## The Effect of Medroxy Progesterone Acetate on the Genital Organ

1] Endometrium:

In patients receiving medroxyprogesterone acetate there were moderate to marked reversible changes on vaginal cytology with a decrease of superficial cells and karyopyknotic index.

Such effect is more marked when higher doses of medroxyprogesterone acetate are used on lactating women (Zanartu, 1966).

Mishell et al., 1968, found that the karyopyknotic index were low in 100 post-partum women injected with 150 mg medroxyprogesterone acetate once every three months. It was always less than 10%. The percentage of basal cells was also constantly very low, less than 5. Most of the cells found in the vaginal smear at all times throughout the study were of the intermediate type.

El Sheikha (1970) reported that vaginal smears did not show any cyclic variation from week to week or from month to another during the 5 months period following each 400 mg medroxyprogesterone acetate (M.P.A.) injection. There was midzonal shift of the maturation index (M.I. = 0/100).

At the sixth month the smears of 20% of cases showed some superficial cells, however, the karyopyknotic index ranged from 1-5%, i.e. M.I. = 0/99/1 and 0/95/5 respectively. No cellular



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