EFFECT OF ORAL CONTRACEPTIVES ON THE EYE

THESIS

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(M.Sc.)

BY

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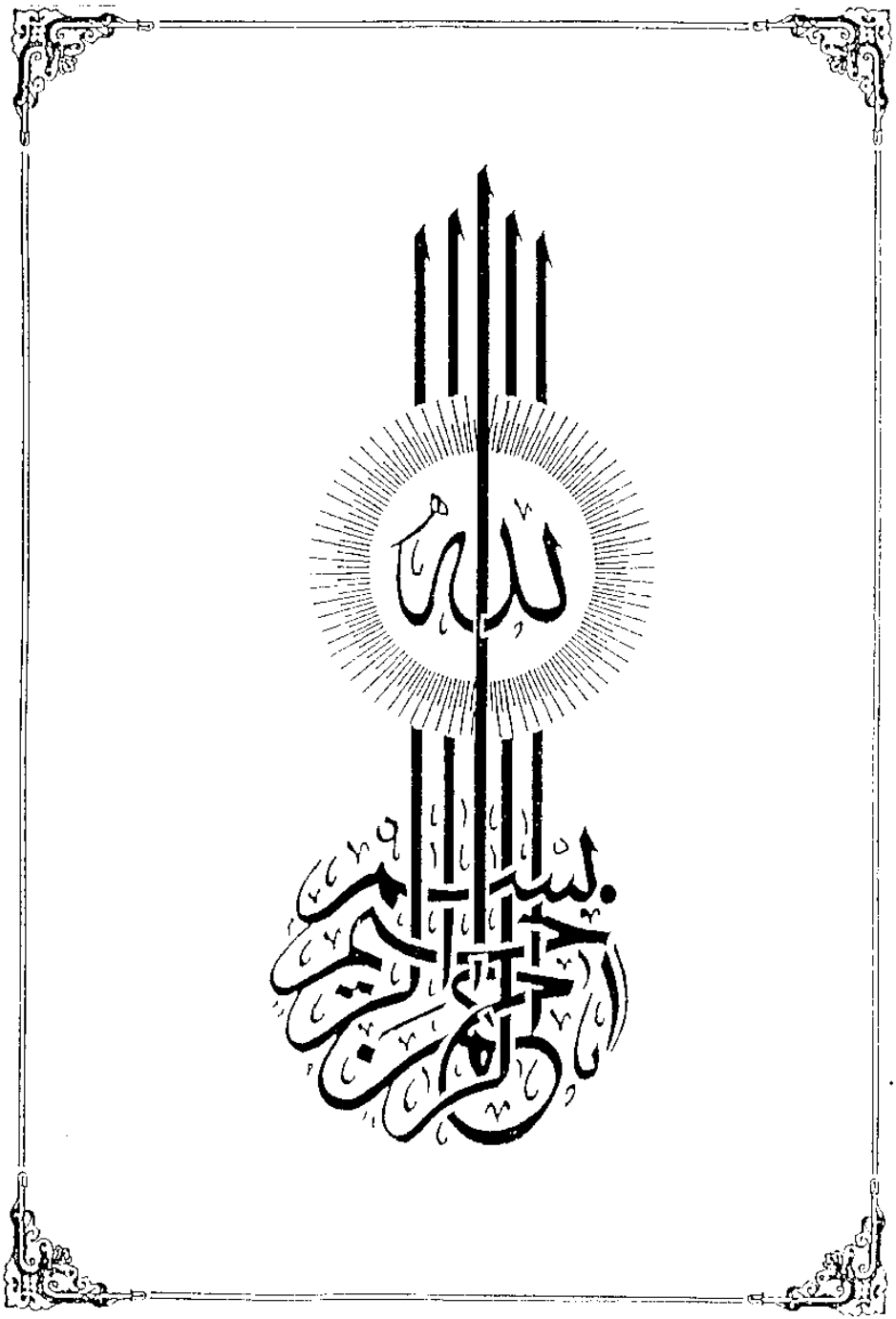

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INTRODUCTION

INTRODUCTION

Egypt is one of the many low-income countries of the world, whose aspiratian for economic development is restricted by rapid population growth.

The population in 1927, 1937 and 1947 were 14.4, 15.9 and 19 million respectively. The census in 1967 was 31.7 million. The death-rate shows a steady decline from 21.4 in 1963, while birth-rate remained stationary almost for the last fifty years, ranging between 41 -44 per thousand (Hefnawi, Kandil, Askalani, Younis, Hasseeb, El-Tagi, and Hosni, 1974). This resulted in an explosive population growth. As a result of the present policy of improving the quality & quantity of free medical services, especially in the rural areas, a more decline in the death rate is anti-cipated which results in more population growth. Hence the only way is to lower the birth rate through control of fertility. Pill is now used by 25-50 million women throughout the world, twenty to forty percent of all fecund women have used oral contraceptives in developed countries in recent years (Hefnawi, et al 1974). The pill affects virtually every organ system. It is those pill complication which became worse overtime which deserve our constant attention as we provide pills to more women who used pills for period of 5-15 years.

The aim of this work is to discuss the different adverse reactions of contraceptive pills on the eye.

HISTORY
AND
DEVELOPMENT.

HISTORY and DEVELOPMENT

Ovulation-inhibiting hormonal contraceptives are oesterogenic or progestional steroids, or a combination of both. Up to 1960, when the first hormonal oral contraceptive was approved by the food and Drug Administration of the United States, development of new chemical contraceptives was slow and lacked originality. Howerer, the introduction of the first oral contraceptive, also dubbed "the pill," stimulated competition between chemists and pharmacologists in the international pharmaceutical research centres to discover hormonal compounds of increased selectivity and boilogical efficacy for new oral contraceptives. Preliminary chemical studies toward the development of highly active, anti-ovulatory steroids were intitiated in the 1930s with the isolation of progesterone the orally active progestin, ethisternoe, and the orally active esterogen, ethinyl esteradiol (Bennett, 1974).

In 1937 Makepeace, Weinstein and Friedman (1937) discovered that progesterone inhibited ovulation in rabbits.

Three years later Sturgis and Albright (1940) found that oestrogen used in the treatment of dysmenorrhoea also inhibited ovulation.

In the early 1950s researh was carried out to develop orally-active progestational steroids to be used to suppress ovulation. Norethynodrel was the first such compound to be synthesised in 1952, followed by norethisterone in 1954 (Hawkins and Elder, 1979).

Norethynodrel is the progestational component of the first oral contraceptive, Enavid (Enovid), which was shown to inhibit ovulation in the rabbit by Pincus, Chung, Zarrow and Hafez (1956) and in the human by Rock, Pincus and Garcia (1956).

The first clinical trials with Enavid were car ied out on Puerto Rican women during 1956 and were followed by more extensive studies(Pincus, Rock and Garcia (1958).

Enavid was marketed for the treatment of menstrual disorders in 1957 and as an oral contraceptives in 1960. The initial dose of norethynodrel was 10 mg, but with the introduction of more effective progestational agents and the realisation that an oestrogen component is the main factor in suppressing ovulation, the hormone content of oral contraceptives has been considerably reduced. Most combined oral contraceptive pills now contain 0.5-2.0 mg of progesterone, some contain as little as 0.15 mg of norgestrel (Hawkins, and Elder 1979).

After Inman, Vessey, Westerholm, and Engelund (1970) suggested that thrombo-embolic side-effects of the combined pill depended on the oestrogen dose, this was reduced from 200 to 100 to 50 mg of ethinylestera-diol or mestranol. Some oral contraceptives now contain as little as 20 µg of synthetic oestrogen. The realisation that oestrogens were responsible for many of the major metabolic side effects of the combined pill caused a return of interest in the study of products containing only progestational steroids. The first such preparation was chlormadinone acetate which became available during the mid 1960s. Tablets containing only norethisterone (norethindrone), ethynodiol diacetate, lynoestrenol, quingestanol acetate, norgestrol or clogestone have subsquently been tried or marketed with varying degrees of success. They are not widly prescribed but are useful for the woman who desires oral contraception and is advised against the use of the combined pill for medical reasons or is reluctant to accept any small risks that might be associated with synthetic oestrogens (Hawkins and Elder, 1979).

PHYSIOLOGY AND PHARMACOLOGY

Physiology and Pharmacology

Scientific Basis of Oral Contraception

A clear understanding of the effects of hormonal contraception and its management in women must be based on knowledge of the mechanism of control of ovulation and the sequence of events in a normal menstrual cycle. In a normal menstrual cycle the occurence of ovulation is influenced both by conscious and unconscious responses in the central nervous system and also by enviromental factors. These effects are mediated by the hypothalmic nerve fibres, which enter the median eminence of pituitary gland and terminate in the hypophysial portal plexus of vessels.The anterior pituitary gland secretes the gonadotrophic hormones F.S.H and L.H which control the function of the ovary. This secretion of F.S.H and L.H by the pituitary is itself controlled by hypothalamic releasing factors F.S.H - RF and L.H - RF. Under the influence of pituitary gonadotrophins the ovaries secret oestrogens and progesterone which act on the reproductive tract to produce changes in the uterus, cervix, and vagina. Most women secret both F.S.H and L.H throughout the menstrual cycle though their levels vary during its different phases. In the early part of each cycle there is a rise in the pituitary secretion of F.S.H, and as the ovarian follicle

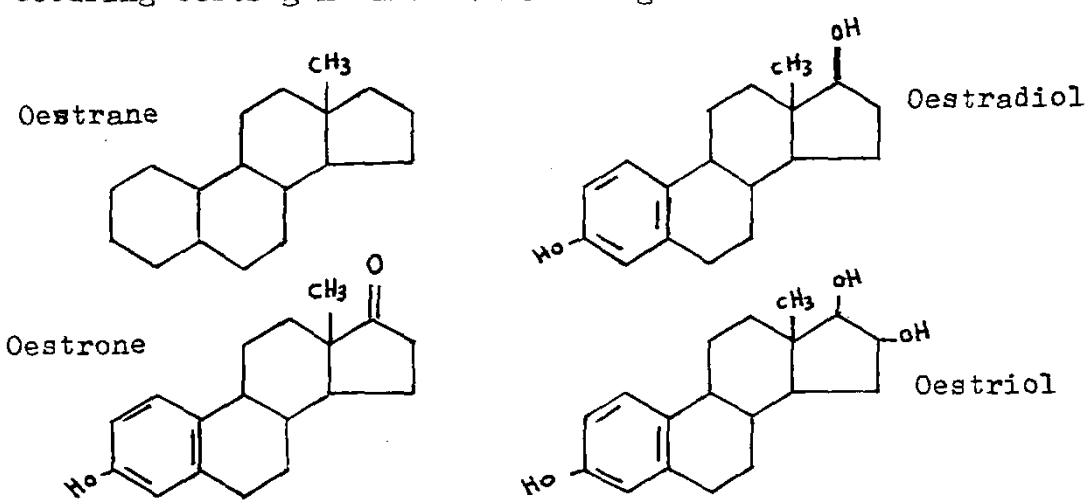
matures in response to this stimulation, it secretes oestrogen. The steadily rising plasma level of oestrogen inhibits F.S.H. production, the processes of biological feedback, and also stimulates the pituitary to step up its secretion of L.H. (Ramaswamy and Smith 1976).

Oestrogen

I. Natural Oestrogens :

Oestrogens are the principal functional hormones produced by the ovarian follicles.They are trophic hormones which play a part in growth and development of the non-pregnant woman, having a specific function in promoting the development of the female genitalia and secondary sexual characteristics.

In the human female the three major oestrogens are, oestradiol, oestrone and oestriol. Oestradiol is the most biologically active of the three, oestriol the least active. They are C-18 steroids, that is derived from oestrane, which has 18 carbon atoms. The formulae of the steroid nucleus and the three naturally occuring oestrogens are shown in figure 2.1 .



(Fig. 2.1)