M E N O P A U S E

ESSAY

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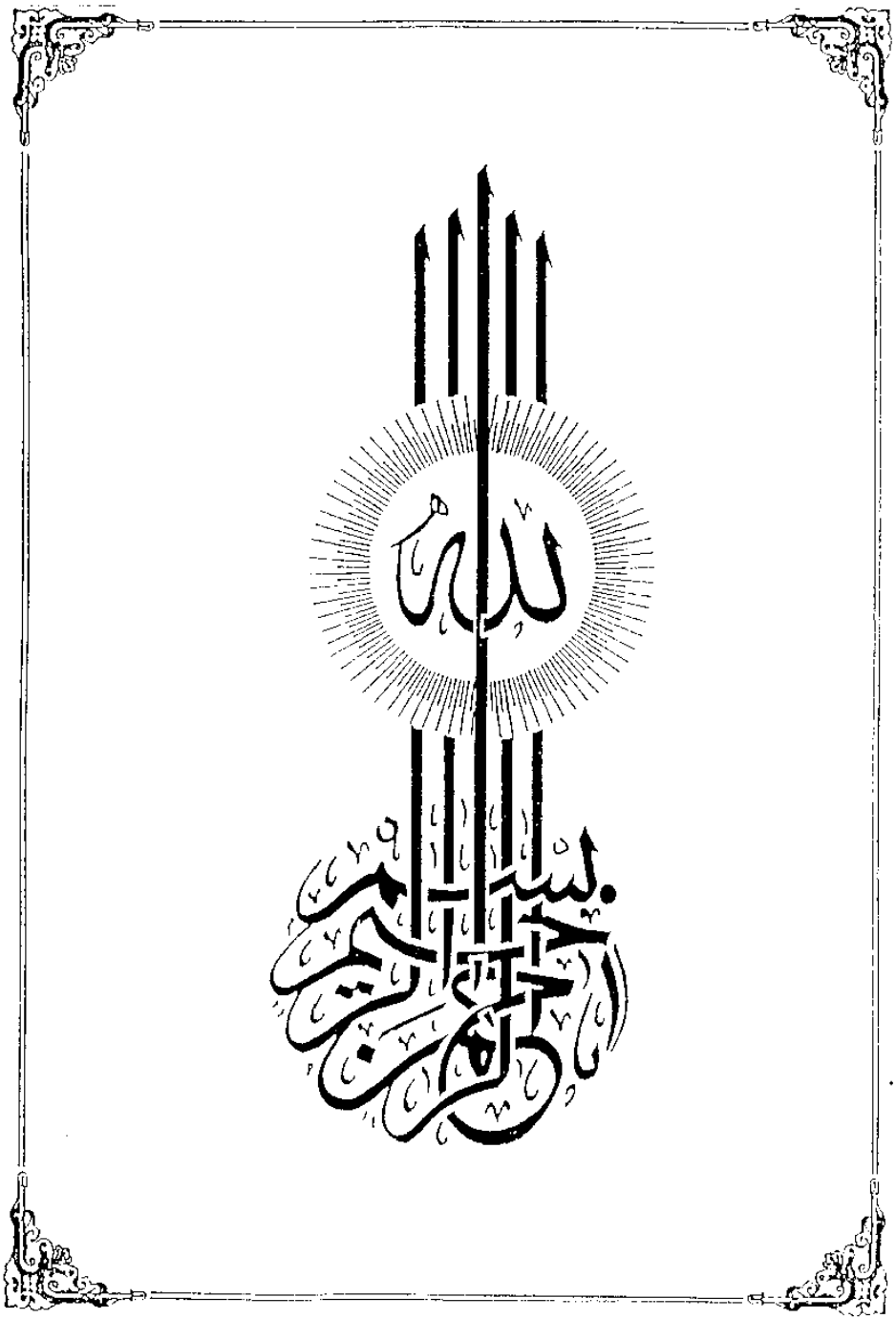

Aim of the Work

The aim of our work is to

Supply the library by an updated Text about Menopause Pathophysiology with special high lights on the new modalities of treatment of the menopause.

Materials & Method

Review all Recent referance, periodicals, and toxtbooks of the menopauose.

P.L. (1975) J. The decline in fertility in most animals is due to hypothalamic. Pituitary dysfunction rather than to ovarian failure as occurs in CBA mice and in man.

The menopause and post-menopause as seen in the human female is an almost unique biological pehnomena.

Life expectancy and age of menopause:

The number of women experiencing and living beyond the menopause has increased slowly over the centuries with the progressive increase in the life expectancy. The average span of life in the Roman times is believed to have bean about 25 years.

It was not until the present century that the average expectation of life reached about 50 years since 1900, however the life expectancy has rapidly increased and is now approaching 75 years in developed countries. It may even reach 80 year 2000. in contemporary developed countries approximately 95% of women line to experience the menopause, 50-60% achive the age of 75 years and third or more of all women are pri or postmenopausal. contrary to beliefs that the age of the menpause is increasing. Amundsen and Diers, who reviewed medieual records from the 6th to the 15 centuries, found that the average age of menopause has remained remarkably constant at about 50 years. (Amundsen D.W. &

Diersc. J. (1975). An earliar menopause an easlietl is associated with cigarette somking and living at high altitudes. (Mckinlay SM, Bifano Nl. Mckinlay JB, Smoking and age at menopause in women, Aun Int. Med. 103:350, 1985).

There is reason to believe that premature ovarain failure occurs in women who have previously undergon abdomenal hyoterectomy, presumably because ovarin vasculature has been compromised. (Siddle N, et al, 1987).

The effect of hysterectomy on the age of ovarin failure: identification of a subgroup of women with premature loss of ovarian function and literature review, Fertil steril, 1987). There is concern at the individual level as well. For some women, menopause signals the beginning of an era of aging with its connotation of diminshing abilities and competance. The menopause however, should and can mark the beginning of an era of aging with its connotation of diminshing abilities and competence. The menopause, however, should and can mark the begining of a new and promising period of life, relatively free from previous obligation, ready for new carrer choices, more education, and new ventures, good medical practice dictates that concerned physican should support falient in positive outlook for this period of time, a period of time which growing in length and should be increasingly productive and rewarding.

Physiology of menestrual cycle :

The physiology of menestrual cycle depend on Dyanamic mechanism between the pituitary and gonadal hormons. This mechanism allow the cyclic nature of normal reproduction processes.

The hormonal changes usually associated with morphlogical changes in the ovary. Making the hormone of this system one of the most remarkable events in biology. The menestrual cycle can divide in to 3 phases: The follicular phase, ovulation and the luteal phase. During the follicular phase there is sequence of events takes place to make some that proper number of follicles is ready for ovulation. and usually the end result of this fallicular development a surviving of one mature fallicle.

This process, which occurs over the period of 10-14 days it is due to a series of actions of hormons on the follicle. This sequential action of hormons on the fallicle marking the follicle destined to ovulat during a period of initial growth from primordial follicle through the stages of preantral, antral and preovulatory fallicle. Primordil follicle consists of an oocyte, arrested in meiotic prophase, surrounded by single layer of granulosa cells. The follicle begin to grow under all physiological

circumstances, on other word not interrpted by pregnancy, ovulation or period of anovulation. Growth contenues at all age, including infaney and around the menopause. It is proved that the number starts to growing each cycle depend upon the size of the residual pool of Inactive follicles. (Peters H, et al 1975). Reducing the size of the pool as in unilateral oophorectomy. Macking the remaining follicles to redistribute their avalability over the time.
The processes which follicles or how many will develop during one cycle is unknown.

It is possible that the follicle which play the leading role in certain cycle its the follicle which timely ready to appropriate tropic hormone stimulation. The first follicle respond to stimulation may achieve an early lead which it never cease. It is clear however that the fallicle distined to ovulate is recruited in the first few days of the cycle (MaisV, et al, 1986). The first sign appear in the new number of follicle is when the granulosa cells become cubidal rather than squamous. At the same time there is a gap junction formed in granulosa celles in respons to fallicle-stimulating hormone FSH. Serve for nutritional and metabolites interchange between the granulosa and oocyt. The initiation of fallicular growth is independant of

gonodotropin stimulation. So the majority of growth follicle has limited growth and followed by atresia.

At the begining of the menstrual cycle the general pattern is interrupted due to respond a group of follicles to a hormonal change and pushed them for further growth. It is happened due to a rise in FSH (accompanied by arise in LH) which save a group of follicles from atsesia. (Vermesh M, Klctzkyoa 1979).

The follicle progresses to pre antral stage once growth is initiated, in these stage thecocyte enlarges and is surrounded by a membrane, the zone pellucida. There is some change in two-cell system, the granulasa cells undergo prolifration and the theca layer begins to organize from the surrounding stroma. This growth dependent upon gonadotropins and associated with increasing production of esterogen. The preantral fallicle can synthesize all 3 classes of steroids from it is granlosa cells; with significantly more esterogens than either androgens or progestins. It appear to be factor limiting ovarian esterogene production by aromatisation of androgens to esterogen. Aromatization takes it is action in preantral granulosa cells by the action of FSH on specific receptors present in this cells which can aromatize limited amount of androgens and generate its

own estrogenic microenvironment. (McNattykp, et al, 1979). Estrogen production depend upon FSH receptor content. FSH recepters appear immediately with inital growth of the follicle, and found that the FSH receptor will rise in concentration after administration of FSH in vivo and in vitro. (EricksonGF, 1986) FSH with esterogen stimulate the proliferation of the graulosa cells. They also promote rapid accumulation of FSH receptors. The appearance of sterogen early in granudosa cells within the follicle allows the folicle to respond to relatively low concentration of FSH, an autocrine function for esterogen within the follicle. Within the follicles not every cell has to contain receptors for the gonadotropins. Cells with receptors causes protein kinase activation in cells which lack receptors. (Fletcher WH, et al 1985).

In early follicular development specific androgen receptors are present in granulosa cells. Androgen in low concentration enhance aromatase activity. Androgen-rich environment, Preantral granulosa cells favor the conversion of androstardione to move potent 5 α -reduced androgen rather than esterogen. (McNattyKP, et al, 1979). and these potent audrogen inhibit aromatose activity. They also inhibit FSH induction of lutenizing hormone (LH) receptor formation,

anther esential step in follicular development. (Jia xc et al 1985.)

The fate of the preantral follicle is in fin balance. At low concentration, androgen stimulate their own aromatization and sheir to sterogen production. At higher concentration has limited capacity of aromatization and the fallicle became atretic. (Erickson et al, 1985).

The success of a follicle depends upon its ability to convert androgen to esterogen. Under the influence of esterogen and FSH increase production of follicular fluid which accumulates in the intercellular spaces of the granulosa, and form activity, which the follicle trnsitian the antral stage. The accumulation of follicular fluid makes the oocyte and surrounding granulosa cells bring up a specific endocrine environment for each fallicle. FSH is essential for presence of esterogen as dominant substance in the follicular fluid. but in the absence of FSH androgens Predominate. (Mcnattykp et al 1979). Until the midcycle the LH is not nromally present in follicular fluid. If LH prematurely elevated in antral fluid the proliferation of granulosa cells decreased, and degenerative changes occur, so intra fallicular androgen level rise. The lowest androgen/esterogen ratio are the most likely to house a

healthyOocyte. In the antral follicle each compartment (Theca and granulosa) has the ability to produce progestins, androgens and esterogens and aromatase activity observed more in granulosa than in the theca.

Well known that LH receptors are present only in theca cells and FSH receptors only on the granulosa cells. Theca tissue under the influence of LH produce androgens, which aromatized to esterogen in the graulosa cells. The acceleration of estrogen production, due to interaction between granulosa and theca compartment is not fully functional until later in antral development. The growing sensitivity to FSH due to the action of FSH and the enhancing influence of esterogen. are responsible for the conversion from androgen to esterogen (a conversion essential for further growth and development). The selection of the dominant follicle depend upon the successful conversion to an esterogen. maks the selection of the follicle distined to ovilate, which makes only a single follicle succeeds. This process of selection is the result of two esterogen action: first due to local interaction between esterogen and FSH within the follicle.

Second due to negative feedback relationship with FSH at the hypothalamic-pituitary level. In the second process

leads to withdraw genadotropin support from less developed follicles. The fall of FSH decrease the aromatase activity and also interupt the proliferation of granulosa cell, and reduce the FSH receptor in granulosa cells, which promot conversion for an androgenic microenviroment. This induce irreversible atretic change. Inspite of negative feedback of sterogen an FSH leads to inhibit the development of all but the selected follicle, the selected follicle remains dependent upon FSH and complete its preovulatory development. This happened as a significant advantage for dominant follice because of a great content of FSH receptor of granulosa cells, and increase of FSH action due to its high of intera follicular esterogen concentration. So the stimulus for aromatization, FSH can be maintained. While its withdrawn from among the less developed follicle. Atrosia among the lesser follicle is seen to parallel the rise of estrogen.

By day 9 the theca vasculesity in the dominant follicle is twice that of other entral follicles. (Zelezhilc Aj, et al 1981) This allow the delivery of genadotropin to the follicle making the dominant follicle to retain the FSH responsiveness and continued development and function dispite drop gonadotopin level. Ovulatory surge and successful corpuse luteum, depend upon FSH induces LH receptor on

granulosa cells of large antral follicles, again estrogen play a role, with increasing concentration of esterogen within the fallicle, FSH changes its action from its own receptor to the LH receptor. The continued response of dominant fallicle despite of decrease level of FSH with high local estrogen, provides a good conditions for LH receptor development. The inhibition of esterogen synthesis prevents FSH. Stimulated increases in LH receptors. (Knechth, et al, 1985) Prolaction is always present in follicular fluid, but no important role in normal ovulatory cycles. Throug the feedback system. The dominant follicle by it is own esterogen and peptide production control its own destiny. Also the cause of lesser follicle is due to it is own environment by alterning gonadotropin secreation through feedback mechanism.

Gonadotropin releasing hormone (GnRH) has obligatory, role in the control of gonadotropin secretion. The steroid and pieptides originiating in the dominant follicle are responsible for a pattern of gonadotropin secreation during menstural cycle, by feedback mechanism.

Experimently suggests that esterogen through its positive feedback mechanism increase in GnRH receptor concentration, while the negative feedback action operates through a

different and uncertain system (Adams TE, et al 1980). Esterogen decreasing both GnKH pulsatile secreation and GnRH pituitary response by its inhibitory effects in both hypothalamus and pituitary.

Progesteron also working as two sites, inhibitory effects on hypothadomic level, and positive action directely on the pituitary.

FSH secreation is very sensitive to negative inhibitory effects of esterogen even at low levels. On other side the effects of esterogen on LH secreation varies with concentration and duration of exposure. at law level esterogen exerts negative feedback on LH. At higher level esterogen exerts a positive stimulatory feedback effect on LH secreation. This mechanism of esterogen feedback on LH from suppression to stimulation occurs as esterodial rises during the midfollicular phase, and it is depend on concentration of esteradiol, and the duration of time which the esterodial elevation is sustained, it is found to be in women that the concentration which exerts positive feedback is over 200 pg/mL and this concentration must sustained for approximately 50 hours.

The gonadotropin are secreated in pulstile pattern with