CORRELATION STUDY FOR DETECTION OF ACCURACY OF (ACCURETTE ENDOMETRIAL SAMPLING KIT) IN SCREENING OF HIGH-RISK PATIENTS

A thesis

submitted for partial fulfillment of master degree in obstetrics and gynaecology:-

BY:-

Dr.NIHAD HUSSEIN HASSAN

Under supervision of:-

PROF. Dr.MOHAMED ISMAIL RAGAB

PROF. OF OBSTETRICS AND GYNAECOLOGY

AIN SHAMS UNIVERSITY

FACULTY OF MEDICINE

and

Dr. MOHSEN MAGID

LECTURER OF OBSTETRICS AND GYNAECOLOGY

AIN SHAMS UNIVERSITY

FACULTY OF MEDICINE

Faculty of Medicine

Ain Shams University

- 1984-

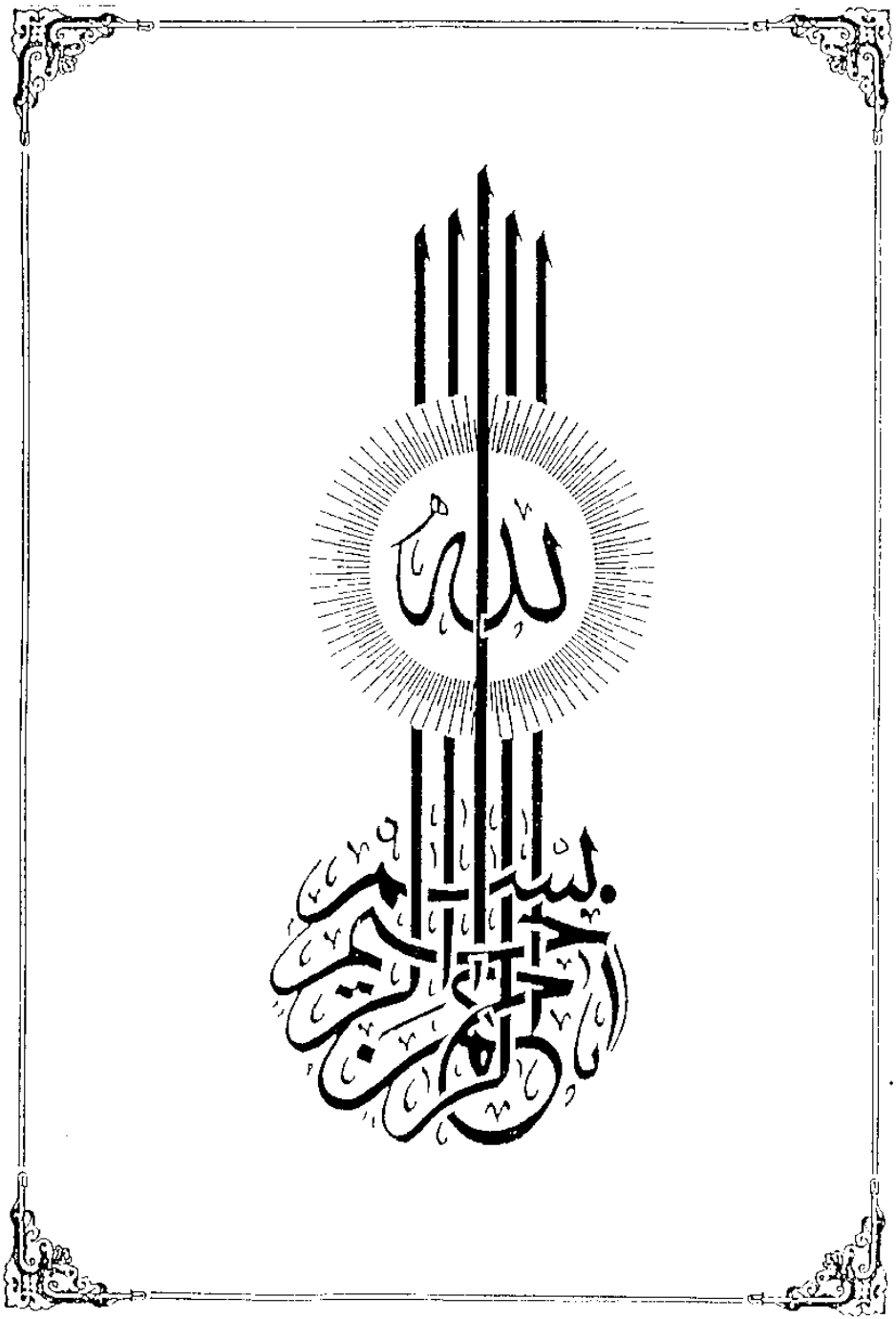
blood supply increases much with prominence of the basal and spiral arterioles especially the latter.

4-Bleeding phase:-

Fanger,and Baker,(1967), stated that shortly before the onset of the menstruation there is intense and prolonged vasoconstriction with resulting ischemia in the endometrial segments supplied.Also there is deterioration of the blood vessel walls which leads to their frequent rupture. This is responsible for the menstrual heamorrhage that occurs when vasoconstriction is followed by a long phase of vasodilatation.So menstruation may thus be a summation of innumerable tiny menstrual heamorrhages in the endometrium supplied by individual spiral arterioles.

Mclennan & Rydell,(1965),said that the tissue loss proceeds in a fragmentory fashion.Rarely the endometrium may be shed in the form of a more or less complete cast. By the third day, the desquamation has commonly reached its limit.The compacta and a variable thickness of spongiosa are usually lost.

Baggish, et al, (1967),stated that even while desquamation is still proceeding,evidances of regeneration of the surface are usually apparent;this takes place from the proliferative, nonsecretory epithelium of the surviving stump of the gland and stroma.



measuring from 5 to 8 mm. in thickness. It is pale , edematous in appearance.The surface epithelium is tall and cylindrical but that of the gland is low.The glands exhibit a steadly increasing tortuosity,the necks being often rather straight and non tortuous, but the middle sections presenting marked scalloping and often a "Saw-tooth" appearance on longitudinal section.The very tips of the glands immediately adjacent to and often dipping into the interstices of the muscle layer commonly show little or no tortuosity.

The basal layer varies much in thickness,sometimes being well marked, in other areas almost absent.

The gland epithelium shows differences in secretory response at the different level corresponding to stratum differences in gland outline. In the middle spongy layer at the greatest tortuosity of the glands,the epithelium is low and pale staining.The nuclei have receded toward the basment membrane.In the basal layer the epithelium shows no secretory responce at all, because the immature epithelium near the growing tips of the gland respond only to estrogen and not progesteron.

The stroma is most abundant in the superficial layer,and shows varing degrees of hypertrophy with broad cytoplasmic zone giving a decidua-like appearance to the cells.The

Regeneration:-

The regeneration of the endometrium is complete and rapid.Complete resurfacing is completed by the fifth day and it is independent of hormonal stimulus.Mitosis is rarely seen at this stage.There may be a metaplastic transformation of stromal into epithelial cells.(Novak&Woodruff,1979).

Electron microscopic studies by Ferenzy,(1976),seem to indicate that regeneration occurs only from the remaining basal glands and surface endometrium without involvement of the stroma.

The endometrium of pregnancy:-

If pregnancy occurs the hypertrophic and secretory changes of the pregravid phase become more marked.The glands present marked saw tooth convolution and scalloping, and the epithelium is low, pale staining and actively secretory.At a later stage the tortuosity of the glands is much less and the epithelium becomes very flat,so that there may be difficulty in distinguishing the glands from lymphatics or venules.

The stromal cells become large and polygonal,with a wide zone of cytoplasm surrounding the nucleus.They now constitute the characteristic decidual cells and are

arranged in mosaic or tile like fashion.They occur in large fields in the superficial compact layer in which the gland elements are sparsest.In the middle or spongy zone the hypertrophy and convolution of the glands are most marked with delicate interglandular septa.The basalis shows no response to pregnancy,the tips of the glands are lined by a cuboidal non secretory type of epithelium.

In less than 25 % of cases of uterine or extrauterine pregnancy the endometrium shows tufting and budding of the glandular epithelium,with slight cellular atypia, hyperchromatism,mitotic activity or other alterations. This is the "ARIAS-STELLA" reaction(Novak&Woodruff, 1979).

Endometrium under progestional therapy:-

There is striking conversion of the endometrial stroma into typical"decidual cells" with simultaneous suppression of glandular components so that they undergo almost complete atrophy.This glandular atrophy affects the functional zone of the endometrium.The basal zone shows only an oestrogen response.This glandular atrophy is much more striking with combined than sequential hormones. (Novack & Woodruff, 1979).

Senile endometrium:-

After the menopause the endometrium may undergo atrophic changes.It becomes thin, the surface and gland epithelium appear low cuboidal and the glands become very sparse. It becomes more and more fibrotic with the years.

The thin senile endometrium is quite prone to infection resulting in the so called "senile endometritis" which may produce postmenopausal bleeding which should be differentiated from the bleeding caused by "endometrial adenocarcinoma".Sometimes there may be typical hyperplasia due to extraglandular production of estrogen,(mainly in adrenal cortex)(Novak & Woodruff, 1979).

Endometrial histopathology in perimenopausal age and beyond

ENDOMETRIAL HISTOPATHOLOGY IN PERIMENOPAUSAL AGE AND BEYOND

Near the menopause there are irregularities in the hormonal balance with partial withdrawal of estrogen.The character of the hormonal transition from menstruating to the postmenopausal epochs exhibits wide variation in different women. (Novak & Woodruff,1979).

Novak and Richardson(1941),reported a variety of patterns other than atrophy in the normal postmenopausal endometrium.They reported an incidence of active hyperplasia in twenty per cent of their cases and proliferative endometrium in a further five per cent.

Macbride (1955), also proved this observation of a normal postmenopausal endometrium.

The commonest functional disturbance is cystic glandular hyperplasia which usually develops during the climacteric period.This is caused by continued extraglandular production of oestrogen while progesterone production gradually diminished(Novak &Woodruff 1979).

Much less common than glandular cystic hyperplasia is the so called "Secretory hypertrophy of the climacterium", described(by Dallenbach _ Hellweg(1981).In this condition endometrial glands are highly secretory,the stroma is predecidual, very loose and focally edematous. It is benign condition, probably produced by over stimulation from excessive pituitary gonadotropins,which cause in turn

hyperactivity of the corpus luteum.Usually this condition disappears at menopause.

Novak &Woodruff (1979), stated that the histologic picture of the postmenopausal endometrium represents the "petrified picture" of the last menstrual cycle that existed when the menopause sets in.So this atrophic pattern may have many forms. If the last few cycles were ovulatory and ended with a regular menstruation, a simple atrophy will develop with few narrow glands lined by a low cuboidal epithelium with small inactive nuclei and supported by dense, fibrous stroma of spindle cells. Spiral arterioles will be lacking.

On the contrary, if the last cycle or cycles were anovulatory,the atrophic endometrium contains some cystically dilated glands,the histologic picture may be misdiagnosed as glandular cystic hyperplasia.However it is evident from the inactive, flattened glandular epithelium that it is a type of atrophy(Dallenbach-Hellweg, 1981).

The interpretation of this inactive dilated glandular pattern is variable. Novak&Richardson(1941), considered it "a retrogressive hyperplasia". Speert (1949), considered it simple "retension cysts" by fibrous stroma. But Novak & Woodruff (1979),and Dallenbach-Hellweg (1981), differentiated between the two conditions,in the first, the main endometrial pattern is atrophic with few glands some of

them are slightly cystically dilated, they explain this dilation by blockage of glands by fibrous stroma and called it "cystic atrophy".The second condition is characterized by numerous large cystic glands explained by a process of"retrogresive hyperplasia ".

The finding of a secretory endometrium in the postmenopausal women although denied(by Novak& Richardson 1944) is still a rare possibility according to(MacBride 1955), and (Novak and Woodruff, 1979).

Novak & Woodruff(1979)found that ovulation was not infrequent in the women over 50 years of age, but it is only sporadically occuring.The associated corpus luteum is insufficient and results in imperfectly developed secretory changes in the endometrium,so pregnancy is extremly rare.

As far as endometrial polyps are concerned they are considered a frequent pathologic finding during the climacteric period.Their development is though to be induced by the irregular stimulation by oestrogen.Bleeding in this condition can not at times be distinguished from that of a more serious condition,so a curettage is indicated in every patient in the climacteric period presented with bleeding,(Dallenbach-Hellweg,1981).

To summerise:-

The postmenopausal endometrium may show any of the following patterns:-

Simple atrophy:-

A thin atrophic endometrium is the most frequent type seen.

Cystic atrophy:-

Slight cystic, dilated, inactive glands are found within simple atrophic endometrium.

Retrogressive hyperplasia:-

Numerous large,cystic dilated ,inactive glands are present.

Active hyperplasia :-

Either diffuse or in scattered patches which are frequently cystic in type.

Various combinations of the above mentioned patterns may occur.(Novak&Woodruff, 1979).

Constitutional risk factors for the development of endometrial carcinoma

CONSTITUTIONAL RISK FACTORS FOR THE DEVELOPMENT OF ENDOMETRIAL CARCINOMA

1-Late Menopause and early Menarche:-

There are much evidences that the menopause may be delayed in the average cases of endometrial carcinoma. (Randall, 1945).

Randall,(1945),found that about 60% of his cases of adenocarcinoma have late menopause after 50 years.But Taylor & Millen, (1938), did not encounter this relationship. MacMahon,(1974), found that those who are in the menopause beyond age of 52 have 2-4 folds risk than who are in menopause at earlier age. Elwood,et al,(1977),found that the risk of endometrial cancer among women whose menopause occurred at the age of "52" or later was "1.7" times the risk of women whose menopause occured before the age of "49". Thomas,(1978), stated that late menopause is a difficult area to evaluate, as prolonged bleeding may be one of the earlier signs of endometrial cancer or hyperplastic condition of the endometrium.

Elwood,et al,(1977), found that women who experience menarche before the age of "12" years have a risk of endometrial cancer "1.6" times that of women who experience menarche at the age of "12" or older.

2-Diabetes Mellitus:-

Diabetes has long been recognised as one of the disease states which may place the patient at high risk of developing endometrial carcinoma.(MacMahon,1974).

Scheffey,and Thudium,(1937) .,reported 11% diabetes in thier series, but they explain this by the presence of obesity in so many patients together with diabetes. But Marble,(1934), belives that diabetes dose not predispose to cancer.

Palmer,(1949),found an incidence of diabetes in cases of carcinoma of the body is 16.9% and Way,(1954),as high as 29%. MacMahon,(1974),found that diabetic subjects increased 2.8 times risk than those who are not diabetic.

The exact relationship of diabetes mellitus to endometrial cancer is a subject of controversy and remains ill defined.(Davies, 1981).

3- Hypertension:-

Hypertension is another illness which has been associated with endometrial carcinoma patients.(Thomas 1978).

The percentage of hypertension among patients with endometrial carcinoma varies greatly from"16.5"to" 78%"(Boutselis, et al, 1963).