THE POSTMENOPAUSAL ENDOMETRIUM

by

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P R E F A C E.

The investigations on which this thesis is based were carried out by me in the Wards and Pathological Department of the Royal Samaritan Hospital for Women, Glasgow, during the years 1950-1953 while I was holding the appointments of Assistant Surgeon and Assistant Pathologist to the hospital.

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INTRODUCTION

The cyclic changes in the endometrium during the reproductive phase of life, together with the mechanism of bleeding at menstruation have been extensively studied and repeatedly described since Hitchmann and Adler's classical researches in 1907. The histological appearances of the endometrium in functional bleeding have also received much attention and attempts have been made to correlate the endometrial pattern with the occurrence of bleeding. There does not appear to have been a proportionate interest in the histological structure of the post-menopausal endometrium; which is surprising in view of the serious import of many changes at this period of life. It seems to have been assumed that the endometrium, like the other genital tract tissues, always undergoes atrophic changes. The traditional conception of the senile endometrium is of a mucosa which has become thin and atrophic, with a few small inactive glands set in a sparse fibrous stroma. The surface and gland epithelium becomes low cuboidal in type and the glands are

of very small calibre.

That this was not invariably so was reported by Novak (1944) who described the occasional presence of cystic glands lined by flattened epithelium. He also referred to the frequent finding in patients long after the menopause of cystic glandular hyperplasia of the endometrium. Speert (1949) noted the occurrence of endometrial polypi. Mention is also made in the literature (Breipohl, 1935) of the finding of secretory endometrium. It is apparent then that the post-menopausal state of the endometrium is not always one of simple atrophy.

These findings are important because in post-menopausal gynaecological disorders, particularly the occurrence of bleeding, considerable emphasis has been laid on the appearance of the endometrium. The bleeding has, in fact, been related to the pattern of the endometrium and particularly to the finding of cystic glandular hyperplasia. Such a conclusion seems unwarranted if the findings of the various authors quoted above are true. Before any interpretation can be made of the endometrial

picture in cases of post-menopausal bleeding it is obviously necessary to determine the various patterns which may be found in the normal post-menopausal patient and to assess their importance.

It has been shown that the post-menopausal endometrium may be stimulated to growth by the presence of oestrogen in the women's body (Geist, 1935; Novak and Brawner, 1934). The administration of oestrogen even to castrated women will produce a typical hyperplasia (Kaufmann, 1934; and Zuckermann, 1937), and the occurrence of hyperplasia of the endometrium in association with granulosa-cell and thecoma-cell tumours of the ovary is good evidence of the responsiveness of the senile endometrium to the ovarian hormones. On this basis it was assumed that post-menopausal bleeding was always associated with hyperplasia and by inference with an excess of oestrogen. So much so that it was suggested (Te Linde, 1936) that when hyperplasia was found long after the menopause, one should look for ovarian tumours - perhaps too small to be recognised on bimanual examination - that are associated with hyper-oestrinism.

However post-menopausal hyperplasia exists in the absence of any such obvious source of oestrogenic stimulation. Moreover hyperplasia is not an invariable finding in cases of functional post-menopausal bleeding. The incidence of hyperplasia in the endometrium associated with benign post-menopausal bleeding is variously estimated at from 10 to 50 per cent., (Breipohl, 1935; Novak and Yui, 1936; Payne, 1937). In addition it is significant that hyperplasia may be present in the endometrium of a woman who has not had any vaginal bleeding since the cessation of menstruation.

It is obvious that several distinct problems exist in relation to the endometrium of the post-menopausal woman. The first controversial point is the incidence of the varying histological patterns of the normal. The incidence of hyperplasia in post-menopausal patients with and without bleeding is uncertain and the significance of its presence is not clear. The final question is the relationship existing between the endometrial pattern and the occurrence of post-

menopausal bleeding, and the mechanism of the bleeding.

Hyperplasia of the endometrium is histologically a frankly benign lesion in most cases. There are a few instances however in which an unusual degree of epithelial proliferation is present, and in others the glands themselves may show a marked increase in number with almost no interglandular tissue and perhaps with very atypical gland involutions and convolutions. The degree of activity may on occasion suggest actual adenocarcinoma of the endometrium. Such cases are very infrequent and represent only a small percentage of the total. The fact that they do occur has led some observers to suggest the possibility that the two lesions have a common origin and that in fact hyperplasia may be the forerunner of endometrial carcinoma. That natural oestrogens are of similar chemical constitution to some of the known carcinogenic substances raises the question as to whether the oestrogens may not, under certain circumstances, be involved in the aetiology of malignant disease of the endometrium. It is maintained by others, however,

that carcinoma arises in the endometrium as a result of causes as yet unknown, and from start to finish possesses its original malignant histological and biological characteristics.

Any relationship between endometrial hyperplasia and carcinoma might be assessed in several ways. If carcinoma is preceeded by hyperplasia then in such cases the uninvolved portion of the endometrium ought to show hyperplasia. This finding was reported by Novak and Yui (1936), and Payne (1937). Contradictory results have been described by Heurlin (1911); Fahlund and Broders (1946); and Jones and Brewer (1941), who found the associated endometrium to be atrophic in most cases.

Similarily if post-menopausal hyperplasia of the endometrium is a precancerous condition then a follow-up study of such patients should show a significant number of cases developing endometrial cancer as described by Rigo, Scipiades and Vacyz (1950). Hintze (1929) and Winter (1950) on the other hand did not find this to be the case.

This is a matter of extreme clinical importance in the treatment of patients beyond the

menopause where at curettage hyperplasia of the endometrium is discovered. If the histological picture is frankly benign, as it is in most cases, and if there is no close relationship between hyperplasia and carcinoma, then it would seem that curettage would, in addition to supplying the diagnosis, constitute adequate treatment. If however hyperplasia is to be regarded as a pre-cancerous condition in a large proportion of cases then more radical surgery is indicated, and hysterectomy would be necessary. The gynaecologist would require to be convinced beyond reasonable doubt of the malignant potentiality of hyperplasia before abandoning the more conservative approach to the treatment of post-menopausal hyperplasia of the endometrium.

Thus a study of the literature on the subject shows considerable difference of opinion as to the normal variations of pattern in the post-menopausal endometrium. The manifestations of hyperplasia, whether generalised or focal, as in a polyp, do not appear to have received adequate attention and their significance is as yet unestablished. The interpretation of the significance of the finding

of polypi is not clearly established. The incidence of hyperplasia in patients suffering from bleeding is the subject of diverse view and its relationship to bleeding is not uniformly interpreted. The final question is the possible link between endometrial hyperplasia and carcinoma.

There are two additional points of minor importance in connection with the thesis but of major clinical importance. One refers to the state of nutrition of the vagina in patients suffering from endometrial carcinoma. The presence of atrophic vaginitis, suggestive of oestrogen deficiency, in such cases is an anomalous finding in view of the current belief that carcinoma is preceded by hyperplasia which in turn is related to hyperoestrinism. The treatment of hyperplasia and its efficacy as shown in a follow-up is of interest in that it throws light on the nature of the hyperplasia.

SECTION 1

NORMAL POST-MENOPAUSAL ENDOMETRIUM.

At a varying time after the menopause the endometrium is deprived of the stimulation of oestrogen and in many cases becomes thin and atrophic. It has been noted by some observers however that in certain instances the endometrium is relatively abundant. Payne (1937) found post-menopausal hyperplasia in 38 cases, in 25 of which there was no obvious source of oestrogen. In one third of this series there was no history of bleeding after the menopause. Novak and Richardson (1941) studied the endometrium from 78 post-menopausal women in whom bleeding was not a symptom. They noted the following endometrial patterns: atrophy 33 times, "retrogressive hyperplasia" 25 times, hyperplasia 16 times and proliferative on 4 occasions. The term "retrogressive hyperplasia" was applied to an endometrium showing a"Swiss-cheese" pattern but where the appearance was inactive. Gianaroli (1947) reported the frequent finding in the post-menopausal endometrium of cystic glands, sometimes uniformly present but in 15 per cent. of cases

crowded into a localised area of the cavity, especially near the fundus of the uterus, forming polypoidal growths. Speert (1949) examined 60 uteri removed from patients whose only gynaecological abnormality was a prolapse. He found cystic glands in 72 per cent., and in 16.6 per cent. of cases an endometrial polyp containing distended glands was present.

Materials

Specimens obtained by curettage.

In the first instance an analysis was made in 1521 post-menopausal patients not suffering from bleeding who had been curetted in the Royal Samaritan Hospital for Women, Glasgow. Care was taken in the selection of the type of case studied and all cases of functional disorder were eliminated. Only cases where the patient was aged over 40 years and with a history of amenorrhoea for at least a year were included in the investigation. In most cases the patient suffered from prolapse and routine curettage was performed before operation for the cure of prolapse was undertaken. The complaints from which the patients suffered were:-

Prolapse	1503
Abdominal pain	10
Abdominal swelling	4
Backache	4

Findings

In 1315 cases no material beyond a little mucus was obtained at curettage. The total number of cases where curettings were available for examination was 206 and the incidence of the endometrial pattern is shown in Table.1. In one instance there was a tuberculous infection of the endometrium and the glands were so fragmentary it was impossible accurately to allocate it to one of groups.

Table 1

Endometrial pattern in curettage specimens.

Type of Endo-metrium	Atrophic	Inactive dilated gland		Hyper-plasia	Pro-liferative	Fibro Adeno-matous Polyp
		Polyp	Diffuse			
No. of Cases	65	80	8	26	12	14
Percent-age	31.7	39.0	3.9	12.7	5.9	6.8

1. Atrophy. A histological diagnosis of atrophy of the endometrium was based on the finding of a thin mucosa with few small glands in a fibrous

stroma. The diameter of the glands was in the neighbourhood of 0.1 millimetre and the average thickness of the endometrium was 0.4 millimetre. The gland epithelium was low cuboidal in type and inactive in appearance. The histological appearance of the atrophic endometrium is shown in Fig.1.

2. Inactive dilated gland pattern. Two varieties of this change were found. In 80 cases the appearances were confined to a single polypoidal portion of the endometrium and in the remainder the condition was more generalised and diffuse. Where a polyp was present the size varied considerably - the largest noted being 1" x ½" x ¼". This condition was diagnosed when the mucosa showed marked cystic dilatation of the glands, the diameter of which varied greatly but was frequently about 1.5 millimetres, only about six such glands being present in the average low-power field. The cells lining the glands were flattened and inactive in appearance. The glands frequently contained amorphous material of a mucoid nature and disintegrating epithelial cells were also present in many cases. The stroma

Figure 1.

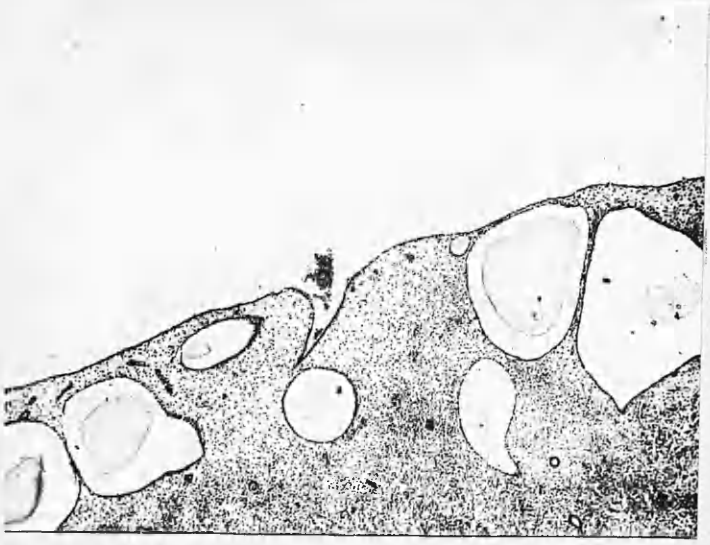
Atrophic Endometrium.

H & E x 50

stained pink with eosin. It was rather less cellular than that characterising the child-bearing years, and the cells were spindle-shaped. No structures recognised as spiral arteries were seen but thin-walled veins and dilated capillaries were present, some of them just beneath the surface epithelium which was low-cuboidal or even flattened. This pattern is illustrated in Figs. 2 and 3.

3. Active hyperplasia. Active hyperplasia of the endometrium was characterised by an increased thickness of endometrium with numerous glands and a very cellular stroma. The glands showed a marked variation in size with dilatation in some, similar to that seen in the active phase of metropathia haemorrhagica. They were considerably smaller than those seen in the inactive gland pattern, varying in diameter from 0.2 to 0.5 millimeter, the endometrium being up to five millimetres thick. In the average case about 20 glands could be found in a low-power field. The glands were lined by a tall columnar epithelium with basophil cytoplasm and large nuclei. There was enlargement of the stromal cells and the cells of both glands and stroma showed frequent mitotic figures. It differed from

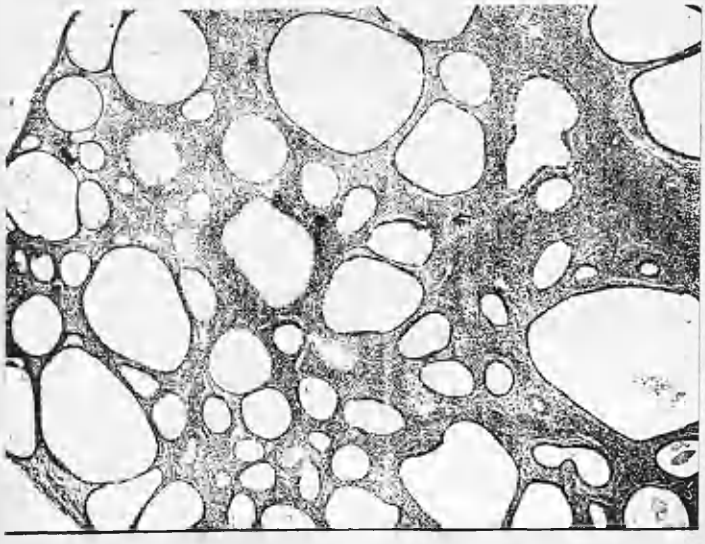
Figure 2.



Inactive dilated gland pattern - diffuse.

The glands are cystic and lined by flattened epithelium.
H & E x 50.

Figure 3.



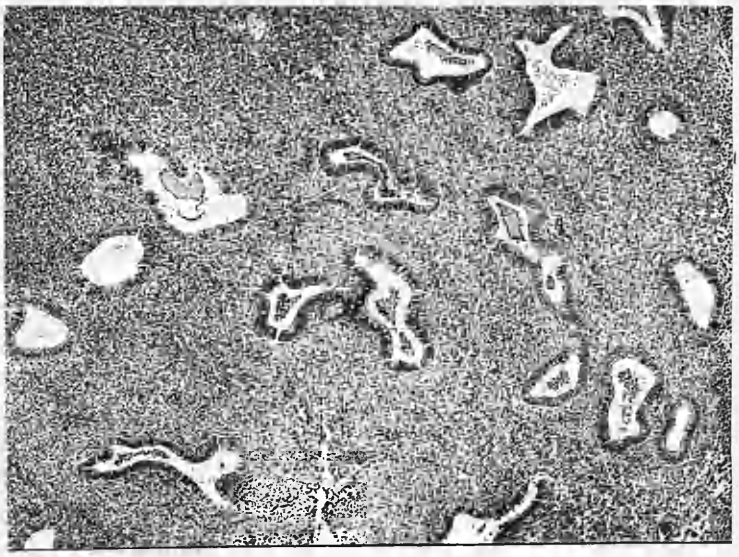
Inactive dilated gland pattern - polyp.

Similar histological appearance to the diffuse variety.-
H & E x 30

cystic glandular hyperplasia of the reproductive period in that areas of stromal haemorrhage and necrosis were absent. In some cases cystic dilatation of the glands was not a prominent feature and the glands tended to be closely packed together with little intervening stroma. Of the 26 cases showing this pattern a polypoid arrangement was noted in 7 instances. The microscopic features are shown in Figs. 4 and 5.

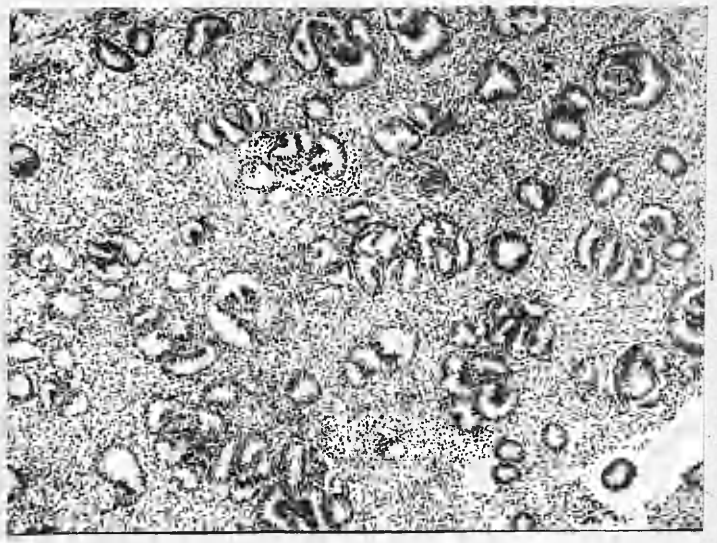
It is important at this stage to differentiate the appearances of polypoid active hyperplasia from these found in polypi of the inactive type. The latter are usually very much larger and in most instances occur singly in the uterus. The glands are on the average more than three times as large as those seen in active hyperplasia. Moreover the general appearance is one of inactivity, there being an absence of mitotic figures in both gland and stromal cells. In most cases the senile polyp is the only tissue removed at curettage. In active hyperplasia, however, several polyps may be removed together with hyperplastic endometrium which represents the rest of the endometrial lining of the uterine cavity.

Figure 4.



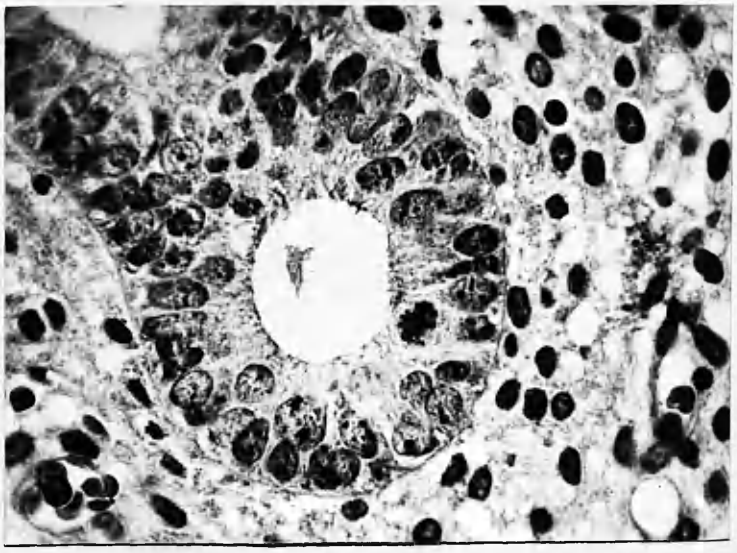
Cystic glandular hyperplasia.
H & E x 75

Figure 5.



Glandular hyperplasia - adenomatous pattern.
H & E x 75

Figure 6.



Mitotic figure in gland epithelium in cystic glandular hyperplasia.

H & E x 700

4. Proliferative endometrium. Proliferative endometrium similar to that seen in the endometrium removed in the first half of the cycle from a woman of the reproductive phase was observed 12 times. Mitotic figures were present in this endometrium but it lacked the disparity in the size of glands seen in the previous type. The glands were about 0.2 millimetre in diameter and the thickness of the endometrium was on the average one millimetre.

5. Fibro adenomatous polyp. The term fibro adenomatous polyp was used to describe polyps in which the stroma was abundant and had a fibrous structure. The cells were spindle-shaped and the matrix was homogeneous and hyalinised. The glands which are of moderate size were lined by cuboidal epithelium. The appearances are shown in Fig.7.

With such a variation in endometrial pattern it might be expected that a relationship to some factor in the patients' gynaecological history would be found. An attempt was therefore made to analyse the results according to the available facts.

Since so many of these patients showed an endometrial pattern which hitherto has been considered abnormal it was obviously necessary to study their menstrual history in some degree at the time of the menopause. The age at which the menopause occurs in a women is to some extent indicative of ovarian activity. This factor is shown in relation to the different endometrial patterns in Table 2. It is obvious that there is no direct relationship between the age of the patient at the time of the menopause and the endometrial pattern found.

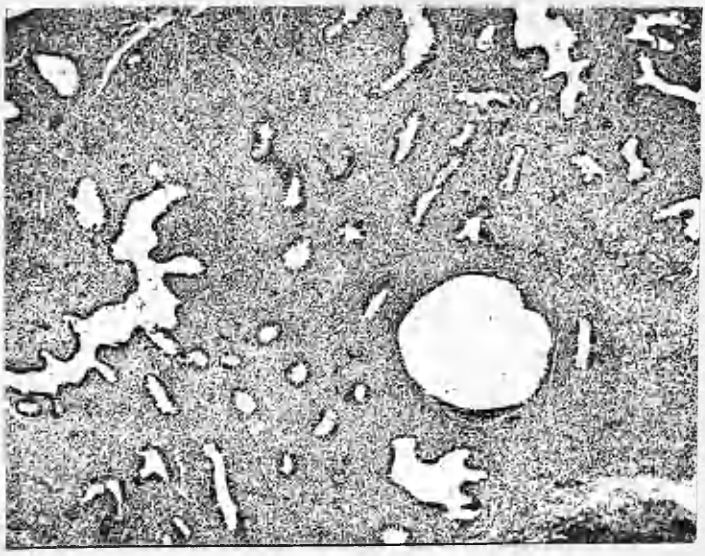
Table 2

Age of menopause in relation to endometrial pattern.

Type of Endometrium	Range	Average
Atrophic	39 - 55	47.8 years
Inactive dilated gland	30 - 55	47 "
Active hyperplasia	40 - 53	48.4 "
Proliferative	37 - 52	47.3 "
Fibro adenomatous polyp	42 - 55	49.6 "

A survey showed that almost all of the patients, irrespective of the endometrial pattern, had had a normal menopause with no untoward symptoms. In three patients the menopause was induced by deep X-ray to the ovaries or intra-

Figure 7.



Fibro adenomatous polyp.

H & E x 30

uterine radium because of excessive bleeding and in a fourth bilateral ovarian cysts were removed and the menopause followed as a result. It can be seen from the distribution that there is no direct connection between the type of menopause and the subsequent endometrial pattern. (Table 3).

Table 3

Type of menopause in relation to endometrial pattern.

Type of endometrium	Natural Menopause	Radium	Deep X-ray	Surgical
Atrophic	64	-	1	-
Inactive dilated gland	86	1	-	1
Active hyperplasia	25	-	1	-
Proliferative	12	-	-	-
Fibro adenomatous polyp	14	-	-	-

In view of the profound changes in the reproductive tract associated with pregnancy and parturition it was felt that a study of the reproductive history of these patients was indicated. It will be seen from Table 4, that there does not appear to be any significant association between the type of endometrium noted in the post-menopausal woman and her reproductive history.

Table 4

Parity in relation to endometrial pattern.

Type of Endometrium	Unmarried	Married but Nulliparous	Parous
Atrophic	2	6	57
Inactive dilated gland	2	12	74
Hyperplasia	-	3	23
Proliferative	1	1	10
Fibro adenomatous polyp	-	-	14

Age after menopause

Curettage in these patients was performed from one to 34 years after the cessation of menstruation. As an endocrine imbalance may be present during the menopause it was considered important to relate the length of time after the cessation of menstruation at which curettage was performed to the endometrial pattern found.

Table 5

Time after the menopause and endometrial pattern.

Years after the menopause	Atrophic	Inactive dilated gland	Hyperplasia	Proliferative	Fibro adenomatous polyp
1-5 years	31.8	23.1	27.5	12.1	5.5
6-10 "	37.2	53.5	-	2.3	6.9
11-15 "	27.6	58.6	-	-	13.8
16-20 "	24.1	65.5	3.5	-	7.
20+ "	38.1	69.1	-	-	-

Inactive dilated gland	
Polyp	Diffuse
21.9	2.2
48.8	4.7
51.7	6.9
58.6	6.9
61.9	-

It will be seen from the table that most cases of hyperplasia and proliferative endometrium occurred in the first 5 years after the menopause. The inactive dilated gland pattern, both in the diffuse form and where a polyp was present, was not so frequent in the early years after the menopause but occurred in a larger proportion of cases in the later years after the menopause.

2. Specimens obtained by hysterectomy.

In order to amplify my observations the endometrium in the excised uterus was studied. It is obvious the removal of the uterus in the absence of functional gynaecological disorder is unusual and only six cases were available for study. The patients who were submitted to hysterectomy complained of the following symptoms:-

Prolapse 3
Abdominal pain 2
Abdominal swelling 1.

In 5 cases the endometrium was found to be atrophic and in the remaining uterus a polyp containing inactive dilated glands was present.

3. Specimens obtained post-mortem.

While a larger number of intact uteri removed at operation might have been obtained from other institutions for study it was felt that no useful purpose would be served. The majority of such specimens are derived from cases of uterine prolapse and it may be argued that this condition is not unassociated with vascular and endocrine changes which might influence the endometrial pattern. As this might give a false impression of the normal, recourse was had to the study of post-mortem material. A total of 100 specimens were obtained. Cardiac failure due to vascular disease, coronary thrombosis or hypertension was responsible for death in 47 of these patients. Post-operative death due to peritonitis or pulmonary embolism accounted for another 26. In 15 cases death was due to carcinomatosis. Six patients died of pneumonia, and uraemia, tuberculosis and diabetes were each responsible for 2 deaths. All of these patients were at least two years past the menopause.

None of them had any symptoms or functional disturbance relating to the genital tract.

The distribution of endometrial pattern in the uteri in this series is shown in Table 6.

Table 6

Endometrial pattern in intact uteri.

Type of Endometrium	Atrophy	Inactive dilated glands	
		Polyp	Diffuse
Percentage	65	15	20

In more than half the cases in which atrophy was noted, an occasional cystic dilated gland was present. It will be seen that the diffuse cystic gland pattern occurred in 20 per cent. of the specimens compared with 3.9 per cent. noted in the series where the diagnosis was made from a study of the curettings. Polyp with inactive cystic glands were found in 15 per cent. of cases, a much lower incidence than was found in the curettage series. There were no examples of active hyperplasia or proliferative endometrium in the uteri obtained at post-mortem.

Study of these specimens gave further information in regard to the group showing diffuse cystic dilatation of glands. In curettage

specimens the impression is that this type of endometrium is bulky but examination of the post-mortem material shows this to be false. Although the cystic glands are large they form superficial bulges on an endometrium which is otherwise very thin and atrophic. Nor do these glands extend in depth into the wall of the uterus. They are purely superficial.

The average age of the patients was 49.7 years, 4 were unmarried, 15 were married but had had no family and 81 were parous women.

Discussion

It will be apparent from the foregoing that there can be a considerable variation in endometrial pattern consistent with a normal post-menopausal history. While three of the patterns described, i.e. atrophic, inactive dilated gland and fibro-adenomatous polypoidal types might be classed together as examples of inactivity, it is surprising to find active proliferation and even hyperplasia in the endometrium of an apparently normal post-menopausal woman. It is perhaps significant that no examples of hyperplasia or proliferative endometrium were found in the uteri of the post-

mortem specimens. With three exceptions all of these uteri were obtained from patients at least 5 years past the menopause. An analysis of the curettage specimens reveals that with two exceptions, hyperplasia and proliferation were only found in the endometrium of patients within 5 years of the menopause.

The term menopause which literally means cessation of menstruation is used also to indicate the transition period between the reproductive era and senesence. And over a period of several years an otherwise normal woman may exhibit symptoms which are in all probability related to endocrine imbalance. Zondek (1934) showed that the initial stages of the menopause are characterised by an increase in the elimination of oestrogen in the urine. Frank (1934) has demonstrated the presence of quite appreciable amounts of oestrogen in the urine and in the blood of patients after the cessation of menstruation. It is possible that when endometrial hyperplasia is found within a few years of the last menstrual period it is due to the persistence of the hyperoestrinism.

No such explanation can be offered for the

single case of hyperplasia occurring 18 years after the menopause. It may be perhaps that the cause in this case was of a similar nature as on subsequent examination the endometrium appeared to be atrophic.

It will be noted from the initial analysis that hyperplasia and proliferation of the endometrium occurred with remarkable frequency in the 205 cases in which the curettings were examined histologically. The absence of examples of these types of endometrium in the uteri obtained at post-mortem suggests that these figures are fallacious and some explanation must be sought for the disparity between the two series. Although endometrial tissue was obtained 205 times, there was a non-productive curettage in a very large number of normal post-menopausal women, and it is obvious that these must be taken into account in the statistical analysis. It would seem probable that where no endometrial tissue was obtained on curettage the assumption that the endometrium is atrophic or inactive is warranted. If the figures for the curettage are analysed in the light of this the incidence of hyperplasia and proliferation of the endometrium

is reduced to almost negligible proportions.

Table 7

Corrected figures for Table 1.

Type of Endometrium	No. of Cases	Percentage
Inactive	1482	97.5
Hyperplasia	26	1.7
Proliferative	12	0.8

In a consideration of the inactive types of endometrium there is an apparent lack of agreement between the incidence observed in the curettage series and the specimens obtained at post-mortem where the whole uterus was available for study. Where curettage did not result in the obtaining of endometrial tissue for examination the presence of mucus was sometimes noticed. It will be remembered that on study of whole uteri the diffuse cystic gland pattern was found really to be atrophic endometrium and I would suggest that where mucoid material is obtained this is due to the rupture of cystic glands by the curette. If this point be allowed it would appear that the incidence of the diffuse cystic gland pattern is much higher than has previously been thought. Instead of 3.9 per cent. it is almost certain that the incidence noted when the entire uterus was

available for study, that is 20 per cent. is the correct one.

Endometrial polypi with cystic dilated glands were found in a very high percentage of curettings namely 39 per cent. This however is obviously much too high a figure. If the non-productive curettage cases are included in the assessment then the figure fell to 5.25 per cent., but it is possible that this figure errs in the opposite direction. These polypi are most frequently found near the fundus of the uterus as is shown by a study of intact uteri, and it is probable that in a large number of cases the curette fails to locate them, or at most scrapes the surface and draws a little mucus from the ruptured glands. The percentage noted in the series of intact uteri, 15, is likely to represent a true incidence and these senile polypi are probably more frequent than is at present suspected.

The fibro adenomatous polyp may well be considered as a small benign tumour rather than an altered endometrial pattern. Its finding is merely incidental and would be likely in any large series.

It would appear then that in any considerable number of post-menopausal patients the endometrium is likely to show a simple atrophic pattern in 62.5 per cent., a diffuse cystic glandular pattern in 20 per cent. polypi with cystic inactive glands in 15 per cent., hyperplasia in 1.7 per cent. and proliferation in 0.8 per cent. of all cases.

The factors responsible for the varying endometrial patterns are obscure. A study of the obstetrical histories of the patients showed that there was no close relationship between the parity of the patient and the histological picture of the endometrium. Similarily there did not seem to be any connection between the type of endometrium met with in the post menopausal period and the age at which the menopause had occurred or indeed the nature of the menopause.

When however the time after the menopause at which curettage was performed was considered the possible explanation for some of the changes became apparent. It has been pointed out that where hyperplasia or active proliferation of the endometrium was discovered, this was noted with two exceptions within 5 years of the menopause.

The inactive gland pattern, on the other hand, apparently occurred more frequently in the later years. This increased frequency of cystic glandular change in the later years may be more apparent than real and this question will be considered in another part of the thesis.

It is surprising that in all the literature relating to gynaecology in the past forty years only three communications deal with the normal post-menopausal endometrial pattern. Of these only two considered the subject as a separate problem. Novak and Richardson (1941) undertook a study of the post-menopausal endometrium as an incidental part of the larger subject of post-menopausal bleeding. They studied endometriums from 137 post-menopausal women; 78 were not suffering from bleeding. In this series they found simple atrophy in 45 per cent., a retrogressive cystic pattern in 24 per cent., hyperplasia in 20 per cent. and proliferation in 10 per cent. The following table is complied from the figures given in their communication.

This gives a much higher incidence of hyperplasia than was found in my cases where

endometrium was available for examination. Moreover Novak and Richardson in their communication took no account of cases where curettage produced no endometrium. As these probably represented an inactive or even atrophic endometrium it would seem that their figures of 20.4 per cent. hyperplasia and 5.1 per cent. proliferative endometrium give an erroneous impression of the actual incidence of activity among post-menopausal women who have not had any bleeding.

TABLE 8A.

Corrected figures for post menopausal patients without bleeding - Novak and Richardson.

Type of Endo-metrium.	Atrophic.	Pro-lifer-ative.	Hyper-Plastic.	Retro-gressive.
No. of cases	33	4	16	25
Per cent.	42.4	5.1	20.4	32.1

endometrial pattern and the time after the menopause that it was discovered is considered. They found hyperplasia 9 times and proliferative endometrium 4 times in women more than 15 years after the menopause. In my own series, cases of hyperplasia and proliferation were, with 2

exceptions, only found within 5 years of the menopause.

Gianaroli (1947) in a study of intact uteri obtained at operation and at post-mortem failed to find hyperplasia of the endometrium. The most frequent finding was simple atrophy with cystic atrophy in the majority of the remainder. This was the description given to the appearance of small cystic cavities which were sometimes spread all over the mucosa and in 15 per cent. of cases crowded into one part of the mucosa forming a polyp. He interpreted the cystic changes as evidence of a secretory activity of the endometrium. Reference was also made to a dilatation of the capillaries of part of the mucosa. He found telangiectasis in 26 per cent. of cases and noted frequent haemorrhage into the endometrium. He was of the opinion that cystic and telangiectiatic change was the result of temporary reactivation of ovarian function.

Speert (1949) examined 60 uteri taken from women whose only gynaecological abnormality was a prolapse. He found cystic glands in 72 per cent. and in 16.6 per cent. of cases an endometrial

polyp was present. The histological description of the polyps show them to be of the inactive cystic dilated gland pattern and the incidence corresponds closely with my own findings. In not a single case did he find hyperplasia. Speert also stressed the vascular pattern of these polyps and noted particularily the presence of veins just below the surface epithelium and between dilated glands and the surface epithelium. As he was frequently unable to trace a connection between the glands and the surface epithelium, he considered the cystic glands to be retention cysts. He explained bleeding from such polyps as being due to rupture of a superficial cyst and subsequent rupture of a superficial capillary.

From my own observations and the above study of the literature it appears that the post-menopausal endometrial pattern is not one of simple atrophy. In any consideration of pathological conditions related to this period of life the incidence of these various patterns must be taken into consideration.

Since this study was completed I have encountered a case of secretory endometrium

occurring one year after the cessation of menstruation. The patient aged 52 years was admitted for operative treatment of prolapse. There was no history of hormone therapy and there had been no bleeding since the menopause. The histological appearances of the endometrium are shown in Fig. 8.

Summary

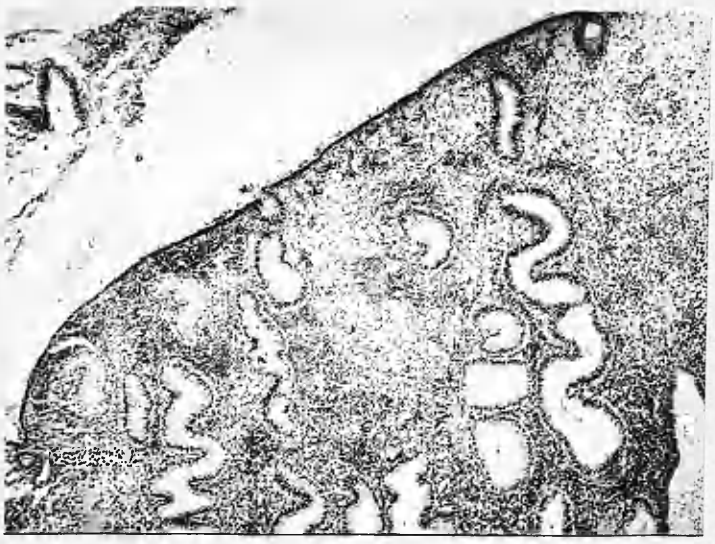
1. A study was made of the endometrial pattern of normal post-menopausal women, both in curettings and in hysterectomy specimens.
2. An inactive endometrial pattern occurred in 97.5 per cent. of cases, hyperplasia in 1.7 per cent. and proliferation in 0.8 per cent.
3. Where an inactive type of endometrium was present, simple atrophy was noted in 65 per cent. of cases.
4. In the remainder, cystic glands were present either diffusely throughout the endometrial lining (20 per cent.), or locally in the form of a polyp (15 per cent.).
5. There was not any relationship between the different types of inactive endometrium and

the time after the menopause at which it was discovered.

6. Active hyperplasia and proliferation of the endometrium, when present, occurred in the early post-menopausal years.

7. Inactivity is the most common condition of the asymptomatic post-menopausal endometrium and the senile endometrial polyp is probably a localised form of one variety of the inactive pattern.

Figure 8.



Secretory endometrium. Sub-nuclear vacuolation is present and the stroma is oedematous.

H & E x 75

Section II.

THE ENDOMETRIUM IN CASES OF POST-MENOPAUSAL BLEEDING

The occurrence of bleeding in a woman some years past the menopause is a dramatic symptom and one fraught with serious danger to the patient's life in many cases. The amount, severity and duration of the bleeding do not seem to be of great diagnostic importance. The appearance of a single spot of vaginal bleeding may be the first indication of a malignant process somewhere in the genital tract. And it is obvious that in an aging population post-menopausal bleeding will become a more frequent gynaecological symptom requiring investigation.

In many cases it is difficult to determine the actual source of the bleeding. In some there may be obvious pathological changes as in cases of cervical polyp, but the appearance on clinical examination does not always suggest that the source of the haemorrhage is to be found in these lesions. Nevertheless it is convenient to consider the subject of post-menopausal bleeding under certain headings and the cases may be divided into five groups as follows:-

A. In a proportion of cases there is a malignant condition of the utero-vaginal tract, commonly of the cervix or the fundus of the uterus.

B. A number of patients have bleeding due to a benign condition of the genital tract outwith the cavity of the uterus.

C. In a few cases the haemorrhage originates in the uterine cavity but some organic lesion of the fundus of the uterus is present.

D. When the above causes of bleeding have been eliminated there remains a large number of patients who bleed from the uterine cavity in the absence of an obvious source of oestrogen and of any pathological condition of the fundus of the uterus. They may be termed cases of "functional" post-menopausal bleeding and it is with this group that I am particularly concerned in this thesis.

E. A small group of patients have bleeding from the uterine cavity and in whom there is known to be an increase of oestrogen either administered medicinally or produced in the woman's body by a granulosa cell or theca cell tumour of the ovary.

Group A - Malignant Disease.

In any case of post-menopausal bleeding, the exclusion of malignancy as a cause is the most important aspect of the investigation of the patient. Malignant conditions are responsible for a high proportion of cases of bleeding in elderly women. Some of the most recent surveys on this subject have assessed the frequency as about 50 per cent. of all cases of post-menopausal bleeding. In the present series of 2062 patients, a malignant condition was found to be present in 27.8 per cent. of such cases. The most common site of carcinoma is the cervix and this condition was found in 14.8 per cent. Carcinoma of the fundus of the uterus was less common but occurred in 8.9 per cent. of the total. In a small number of patients, 3.1 per cent., the tumour was present either in the vulva, vagina, ovary or fallopian tube. In most cases of carcinoma of the cervix curettage of the uterine cavity was not performed and a consideration of the endometrial pattern found in association with endometrial carcinoma forms a later section of the thesis.

Group B - Bleeding from an extra uterine source.

This is a miscellaneous group including decubitus ulcer and pessary ulceration, senile vaginitis and benign conditions of the cervix, e.g. cervical polyps and erosions. Even where such a condition is found on exmination the gynaecologist, if he is wise will explore the cavity of the uterus to exclude the presence of a co-existing endometrial carcinoma. For the most part this was done in the cases studied and usually any endometrial tissue removed by the curette was submitted for histological examination.

In all 573 cases fell into this category. From this series curettage failed to produce endometrial tissue in 474 instances. Analysis of the remaining 99 cases was made on the same basis as described in the previous section of the thesis. Examples of all the types of endometrium previously described were found and the incidence of each type is noted in Table 9.

As previously stated such an assessment must necessarily be inaccurate. The non-productive curettages must be taken into consideration and as before they must represent either cases of complete endometrial atrophy or of those with an

inactive endometrium containing some cystic glands.

Table 9

Endometrial pattern in Group B.

Type of Endo-metrium	Atrophy	Inactive cystic glands	Hyper-plasia	Fibro adenomatous Polyp	Pro-lifer-ative
No. of cases	37	33	16	9	4
Per cent.	37.4	33.3	16.3	9	4

This fact was used in calculating the relative proportion of active and inactive endometrial patterns in normal post-menopausal women and a similar calculation for patients in this group gives the results shown in Table 10.

Table 10

Corrected figures for Table 9.

Type of Endometrium	Inactive	Active
No. of cases	553	20
Per cent.	96.5	3.5

It will be seen that the incidence of hyperplasia and proliferation of the endometrium (3.5 per cent.) is slightly higher than the corresponding figure in the series of post-menopausal women who did not have any bleeding (2.5 per cent.). This increased incidence of hyperplasia may be

entirely fortuitous, but in some of those cases the obvious lesion such as a cervical polyp did not appear, on clinical examination, to be the source of bleeding. In such cases it is possible that the bleeding originated from the endometrium, which would suggest that the increased incidence of hyperplasia of the endometrium may be significant. This however will be considered more fully in a subsequent portion of the thesis dealing with this specific problem. In most instances it would seem that the bleeding in patients in this group was actually caused by the obvious extra uterine lesion, and the endometrial pattern noted corresponds reasonably closely with that found in the post-menopausal woman who does not bleed.

The incidence of varying endometrial pattern in relation to the time after the menopause when curettage was performed is shown in Table 11.

From Table 11 it will be seen that hyperplasia of the endometrium was noted in one third of cases in the first five years after the menopause and approximately one tenth of the total in the later year groups. It should be said however that these percentages represent

relatively small numbers and in fact, of the patients whose endometrium showed hyperplasia or proliferation, 11, or more than half occurred within 5 years of the menopause.

Table 11

Time after the menopause and endometrial pattern.

Years after Meno-pause	Atrophic	Inactive Cystic gland pattern	Hyper-plasia	Fibro-adeno-matous polyp	Prolifer-ative
Under 5 yrs.	29.6	18.5	33.3	11.1	7.4
6-10	42.3	42.3	3.8	3.8	3.8
11-15	36.9	42.0	10.5	10.5	-
16.-20	37.5	37.5	12.5	12.5	-
Over 20 yrs.	33.3	33.3	11.1	11.1	11.1

While analysis of this whole group of cases indicates that the distribution of endometrial pattern does not differ materially from that found in normal post menopausal women, it is conceivable that a change might be associated with one or other particular lesion. The cases formed four sub-groups as follows:-

1. A benign lesion of the cervix, either a polypus, an erosion or chronic cervicitis was presumed to be the cause of bleeding in 15.6 per cent. of cases of post-menopausal bleeding.

A survey of the literature shows that this condition was noted from 6.6 per cent. to 13.9 per cent. of cases (Te Linde 1937; Taylor and Millen 1938; Schwartz 1943; Cheek and Davis 1946). In the quoted series, however, there was no analysis of the type of endometrium found in association with these lesions of the cervix. In my own series, curettings were obtained in 50 cases out of a total of 188 cases. The endometrial patterns found were inactive cystic glands 20 times, atrophy 18, hyperplasia 7, proliferative 3 and a fibro adenomatous polyp in the remaining 2 instances. This represents an incidence of hyperplasia of 3.7 per cent.

2. Prolapse of the uterus complicated by a decubitus ulcer or pessary ulceration was noted in 11.8 per cent. of patients suffering from post-menopausal bleeding. This figure is rather higher than that quoted by the authors mentioned above, whose incidence was from 3.2 to 7.6 per cent. with the exception of Te Linde who noted these conditions in 10.7 per cent. of their cases. As in the other sub-groups there was no analysis of the associated type of endometrium by the authors.

There were 29 specimens of endometrium obtained for examination out of 225 cases, and atrophy was found 9 times, an inactive gland pattern 8, a fibro adenomatous polyp 6, hyperplasia 5, and proliferative endometrium in the remaining case, an incidence of hyperplasia of 2.2 per cent.

3. Senile vaginitis, when present, was characterised by the presence of numerous petechial haemorrhages usually localised to the upper third of the vagina and the vaginal aspect of the cervix. The surface bled when touched and in a few cases the amount of bleeding was quite considerable. This condition was responsible for 9.2 per cent. of all cases of post-menopausal bleeding. The incidence of vaginitis in such cases is recorded as from 1.6 per cent. (Jones and Cantor, 1951) to 11.4 per cent. (Cheek and Davis, 1946). Endometrium was available for study in 18 cases in my series out of 120 cases in all. Atrophy was present in 8 specimens, an inactive gland pattern in 5, hyperplasia in 4 and a fibro adenomatous polyp in the remaining 1. The incidence of hyperplasia was therefore 3.3 per cent.

4. The presence of urethral caruncle was observed

in 3.7 per cent. of post-menopausal bleeding cases. This figure agrees closely with the findings of other writers on this subject who assess the incidence at from 11 to 4 per cent. (Kantor and Klawans 1932; Jones and Cantor 1951). There were 40 cases of urethral caruncle and in the two instances where the endometrium was examined an inactive gland pattern was found.

The incidence of the varying patterns of endometrium found associated with the above gynaecological abnormalities did not show any material alteration from that found in normal post-menopausal women. Consideration of the individual sub-groups might suggest that hyperplasia was unusually common in certain of them but the number of specimens available for examination was very limited, and a true picture can only be obtained by including cases of non-productive curettage. Hyperplasia was not a marked feature in this series of cases and as previously noted an active endometrium was most commonly found in cases within the first five years after the menopause. On consideration of all the facts it would appear that the type of endometrium found in

those post-menopausal patients is not significant and that the bleeding, almost without exception, is derived from the obvious gynaecological lesion.

Group C

It is difficult to assess current opinion on the role of fibroids of the uterus as a cause of post-menopausal bleeding. Most authors dealing with this subject include cases complicated by endometrial carcinoma and many also include cases in which ovarian tumours and fibroids of the uterus occur in the same patient. By calculation from the figures available the incidence of fibroids associated with post-menopausal bleeding given in recent literature varied from 2.8 per cent. (Jones and Cantor, 1951) to 8.4 per cent. (Taylor and Millen, 1938). In the present series I have considered cases in which fibroids were the only abnormality present. The incidence was much lower than that given in other reports, namely 1.9 per cent., representing in all 39 cases.

As hysterectomy had been performed in all cases the endometrium was available for histological examination in every instance. Analysis of the endometrial patterns is shown in

Table 12.

Table 12

Endometrial pattern in cases of fibroid of uterus.

Type of Endo-metrium	Atrophic	Inactive gland Pattern	Pro-liferative	Hyper-plasia	Secre-tory
No. of cases	24	6	4	3	2
Per cent.	61.5	15.4	10.3	7.7	5.1

Only one report deals with the histological endometrial findings in association with fibroids in cases of post-menopausal bleeding. Taylor and Millen (1938) give an account of 28 cases but of these 14 must be excluded because of other possible sources of bleeding. Eight of their cases had an accompanying ovarian tumour, four had a complicating prolapse while in two instances cervical polypi were present.

To date emphasis has been laid mainly in the anatomical position of the fibroid and little attention has been paid to the associated endometrial pattern. Te Linde (1941) while not providing figures, suggests that where post-menopausal bleeding occurs from a fibroid uterus the site of the fibroid was the important factor.

He considered that a submucous fibroid might actually become polypoidal in the post-menopausal period. In 12 of the cases of Taylor and Millen's series the fibroids were submucous and two in the series reported by Cheek and Davis showed polypoidal fibroids. Lund and Dougherty (1950) also refer to the submucous position of the fibroid and suggest that the bleeding arises as a result of necrosis. Geiger (1941) reported 11 cases of fibroids associated with post-menopausal bleeding. Most of these were submucous and a few were pedunculated and presented on the cervical canal. In the present series of 39 cases only 3 were polypoidal.

Nevertheless it is possible as some authors suggest that the mere mechanical presence of a fibroid may induce bleeding. Fibroids even when intramural frequently distort the uterine cavity and cause an increase in the surface area of the endometrium. This of itself would provide a greater surface from which bleeding could occur, but it does not necessarily initiate a bleeding process. It is understandable that in a patient during the reproductive phase of life when the

endometrium is subject to cyclical stimulation and variations, such an increase in surface area would tend to increase the menstrual loss. Fibroids, however, are not invariably associated with abnormal bleeding even in the reproductive period. This suggests that the cyclical stimulation of the uterus in those cases where excessive menstruation is a feature is at least as important as the presence of a fibroid. In other words the fibroid tumour, per se cannot be considered as a direct cause of the uterine bleeding. That this is so is seen in the post menopausal era. Many patients have fibroids of the uterus and do not suffer from bleeding, their only complaint being of a swelling of the abdomen. Where bleeding occurs some additional complication must be present. In a number of cases this may be a polypoidal condition of the tumour with subsequent circulatory disturbance but in others the possibility of a functional upset must be considered. If the cases of fibroids complicated by the presence of an ovarian tumour, prolapse and cervical polypi are eliminated from Taylor and Millen's series then we find that hyperplasia of the endometrium

was encountered in almost 15 per cent. of cases.

An active endometrium was found in 23 per cent. of our cases, 7 per cent. of the total being hyperplastic. This suggests that the endometrium was subject to abnormal stimulation in these cases. There remains however the difficulty of explaining the mechanism of bleeding in those cases where the endometrium was atrophic. This question will be left to be dealt with in a later part of the thesis where the endometrial pattern in cases where the uterus is known to be under the influence of a specific stimulation will be considered.

Group D - "Functional" post-menopausal bleeding.

When the cases of post-menopausal bleeding in which there is an extra uterine cause for the bleeding and those in which there is some pathology of the uterus or ovary present are excluded, there remains a group of cases which may be termed functional post-menopausal bleeding. This is a most interesting group since a study of them may be the means of providing a reasonable interpretation for the endometrial changes in other groups. There were 537 such cases in this series. No

endometrium was found at curettage on 198 occasions. The variation in endometrial pattern in the remainder is shown in Table 13.

Table 13

Endometrial pattern in functional postmenopausal bleeding.

Type of Endo-met-rium	Atrophy	Inactive gland pattern	Hyper-plasia	Pro-lifer-ative	F.A. Polyp	Secre-tory
Total No. of cases	99	82	110	25	15	8
Per cent.	29.2	24.2	32.4	7.3	4.4	2.4

Following the procedure adopted previously, the non-productive curettages may be taken to represent an atrophic pattern with or without cystic dilated glands. The relative numbers of active and inactive patterns may be assessed as shown in Table 14.

Table 14

Corrected figures for Table 13.

Type of endometrium	No. of Cases	Percentage
Inactive	394	73.4
Hyperplasia	110	20.5
Proliferative	25	4.6
Secretory	8	1.5

It will be seen from the above table that hyperplasia was present in about a fifth of all

cases and that an inactive endometrium comprised approximately three quarters of the total.

Secretory endometrium

The appearances in these specimens were essentially similar to those seen during the second half of the cycle during the reproductive period of life and do not necessitate detailed description. There were eight examples of this endometrial pattern in the cases of functional post-menopausal bleeding. In this group the time after the menopause was from one to six years and the ages of the patients ranged from 40 to 52 years. One patient, aged 42 years, had had a menopausal dose of deep X-ray therapy for abnormal uterine bleeding two years previously.

Hyperplasia of the endometrium was formerly considered to be a disease of reproductive life and it seemed reasonable to assume that some relationship might exist between the incidence of post-menopausal hyperplasia and the menstrual history of the patient. An analysis was therefore made of the type of endometrium found in these cases in relation to date at which menstruation ceased and the type of menopause experienced by

the patient. The results of this analysis are seen in Table 15.

Table 15

Age of menopause and endometrial pattern.

Type of Endometrium	Range of age at which menstruation ceased	Average age
Atrophic	From 21-59 years	47.3 years
Inactive gland pattern	" 38-54 "	48.1 "
Hyperplasia	" 36-54 "	47.3 "
Fibro adenomatous polyp	" 38-54 "	47.0 "
Proliferative	" 41-63 "	47.2 "

The only 2 cases in which menstruation ceased before 35 years occurred in women who had had a bilateral oophorectomy performed on account of cysts of the ovaries. There was only one patient who menstruated regularily after the age of 55 years and she experienced the menopause at 63 years. The endometrium obtained in the post-menopausal period when she had some bleeding was of the proliferative pattern.

It will be seen from the table that there is no direct relationship between the type of endometrium found and the age at which the menopause occurred. Nor is there any significant difference

in comparison with the age at which the menopause occurred in women who do not later suffer from post-menopausal bleeding (See Table 2).

It might well be that these symptoms in the post-menopausal phase are merely a carry-over from a similar complaint during the reproductive phase. If such were the case one might reasonably expect that a considerable number of patients would have had some form of treatment particularly the induction of an artificial menopause. The type of menopause experienced by the patients in relation to the endometrial pattern found in functional post-menopausal bleeding is shown in Table 16.

Table 16

Type of menopause and endometrial pattern.

Type of Endometrium	Natural	Artificial		
		Deep X-ray	Radium	Surgical
Atrophy	87	5	3	4
Cystic gland pattern	75	4	1	2
Hyperplasia	106	3	-	1
Fibro adenomatous polyp	13	1	1	-
Proliferative	24	-	1	-
Secretory	7	1	-	-

While the numbers involved are small it would seem that an artificial menopause occurred relatively

oftener in cases showing atrophy or cystic gland pattern then in patients showing hyperplasia. When a comparison is made with normal post-menopausal women there is a higher incidence of an artificial menopause in those patients who suffer from bleeding in the post-menopausal era (6 per cent. compared with 1.5 per cent.) but this incidence is still relatively small and cannot be considered an important factor. It is obvious that in the majority of cases bleeding in the post-menopausal phase is a condition arising de novo. Not all patients who had an artificial menopause necessarily had hyperplasia of the endometrium at that time as it would seem that hyperplasia is present in only a third of cases of functional bleeding of the reproductive period of life.

In four cases where there was a history of excessive menstruation details of the curettage during the reproductive period were available. The first patient aged 42 was curetted because of profuse and irregular bleeding for two years. Only scanty curettings were obtained and were not sent for histological examination. A menopausal dose of deep X-ray to the ovary was given. When the

patient was readmitted to hospital three years later because of bleeding of one month's duration active hyperplasia was found. Similar findings were noted in a second patient with the exception that the interval between the menopausal dose and subsequent bleeding was two years. In the other two patients bleeding at the time of the menopause was treated by curettage - the endometrium was noted to be thickened and on histological examination well marked cystic glandular hyperplasia diagnosed. Four years and 11 years later respectively the patients suffered from post-menopausal bleeding and active hyperplasia of the endometrium was found when curettage was performed. It is apparent even from this small group of patients that the endometrial pattern found in the post menopausal phase bears little relationship to that existing during the reproductive years of life even when the patient has had a similar complaint in both periods.

In view of the possible effect of pregnancy on the hormonal balance of a woman and of possible endocrine imbalance in patients suffering from sterility an analysis was made of the marital status and parity of patients relative to the

endometrial pattern present. The findings are shown in Table 17.

Table 17.

Parity in relation to endometrial pattern.

Type of endometrium	Unmarried	Married but without family	Parous
Atrophy	2	3	94
Cystic gland pattern	4	10	68
Hyperplasia	3	4	103
Fibro adenomatous polyp	1	2	12
Proliferative	1	-	24
Secretory	-	-	8

There is a larger number of unmarried and nulliparous women among the patients found to have an inactive gland pattern - a finding which is in close agreement with the figures obtained in the corresponding analysis for normal post-menopausal women. There does not however, appear to be any relationship between nulliparity and functional post-menopausal bleeding. The majority of patients were parous and there was very little real difference between the various groups.

If endometrial hyperplasia is found shortly after the menopause it may be the persistance of a menopausal condition due to the recent endocrine

imbalance. It was found in the study of normal post-menopausal women that active hyperplasia of the endometrium was noted almost without exception within five years of the cessation of menstruation. It was therefore judged important to assess the incidence of the varying endometrial patterns in relation to the length of time after the menopause that it occurred in patients with bleeding. The findings are seen in Table 18.

Table 18

Time after menopause and endometrial pattern.

Years after the menopause	Atrophic	Cystic gland pattern	Hyper-plasia	Pro-lif-erat-ive	Fibro adeno-matous polyp	Secre-tory
Under 5	33.5	14.8	32.9	10.7	3.4	4.7
6-10	23.1	32.0	30.8	6.4	6.4	1.3
11-15	29.3	21.9	43.9	4.9	-	-
16-20	26.3	34.2	23.7	2.6	13.1	-
Over 20	25.7	40	28.6	5.7	-	-

It is obvious from the above table that hyperplasia and proliferation of the endometrium are by no means confined to the early years after the menopause and indeed may be present over 20 years after the cessation of menstruation. There were 60 cases more than five years after the menopause as follows:- 6-10 years 23; 11-15 years 18;

16-20 years 9; and over 20 years 10. Thus active hyperplasia in the post-menopausal era associated with bleeding is frequently found many years after the menopause. The findings become more striking when these figures are compared with those found in a study of normal post-menopausal patients.

Infection of the Endometrium.

The organisms most frequently responsible for endometritis are various strains of streptococci, often anaerobic, staphylococci and the tubercle bacillus. The chronic phases of inflammation are far more frequently observed in the endometrium than the acute. In the senile variety the endometrium is frequently thin and atrophic and heavily infiltrated with round and plasma cells (Novak 1944). Ulceration of the surface may occur causing post-menopausal bleeding. In cases of tuberculous endometritis one may find only an occasional tubercle, or cluster of tubercles with the characteristic epithelial and giant cells and where the disease is extensive caseation is present to greater or less degree.

Pyogenic endometritis

Chronic pyogenic infection of the endometrium was encountered 23 times where post-menopausal bleeding had occurred from a grossly normal uterus representing 4.3 per cent. The infective process was not limited to endometrium of an atrophic type and its incidence in relation to the different endometrial patterns is shown in Table 19.

Table 19.
Infection in relation to endometrial pattern.

Type of Endometrium	Atrophic	Inactive gland pattern	Hyper-plasia	Pro-liferative	Fibro adeno polyp
Total No. of cases	99	82	110	25	15
No. of cases showing infection	8	8	5	1	1

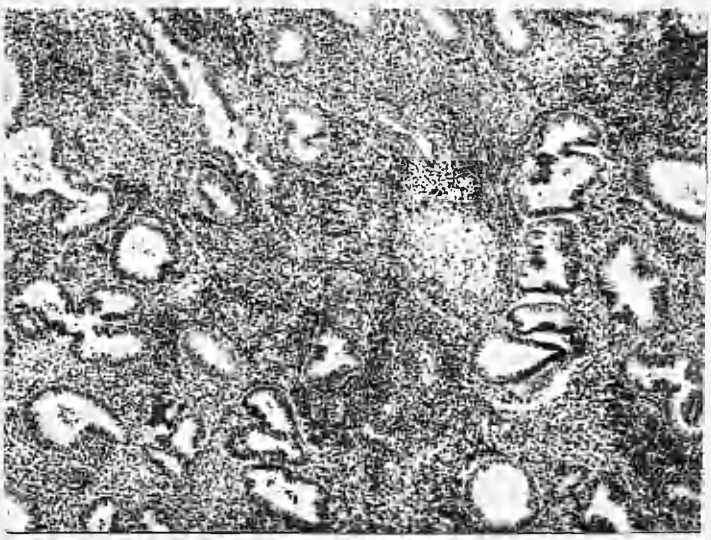
It would appear from the above table that infection is relatively more frequent where the endometrium is either atrophic or inactive.

Tuberculous infection

There were six cases of endometrial tuberculosis in post-menopausal women complaining of bleeding.

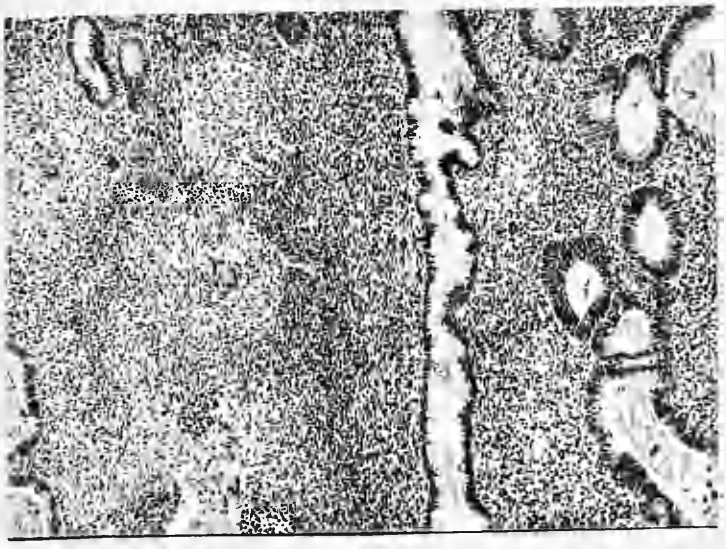
One patient five years after the menopause had a hysterectomy and bilateral salpingo oophorectomy performed. The endometrium was

Figure 9.



Cystic glandular hyperplasia in patient suffering from bleeding fifteen years after the menopause.
H & E x 75

Figure 10.



Tuberculous infection of endometrium showing cystic glandular hyperplasia.
H & E x 75

thickened and filled the uterine cavity while the tubes were also thickened. Histological examination showed a cystic glandular hyperplasia associated with a definite tuberculous infection. Bilateral tuberculous salpingitis was also present. The appearances are illustrated in Fig.10.

In two cases there was a tuberculous infection of endometrium similar to that of the proliferative phase in the reproductive life.

There were two cases of a severe tuberculous infection of an atrophic endometrium.

The other patient suddenly developed a heavy white vaginal discharge five weeks before admission and eight years after the menopause.
Vaginal bleeding followed examination in the out-patient department. When the cervix was dilated large quantities of thick creamy pus poured from the uterus. A week later a catheter was inserted into the uterus and stitched in position to allow drainage of the pyometra. When curettage was eventually performed, tuberculous granulation tissue was obtained.

Discussion

There is an extensive literature on the subject

of post-menopausal bleeding though naturally much of it is concerned with the incidence of malignant conditions. Even where benign lesions are dealt with there is frequently little description of the histology of the endometrium and attention is focussed on obvious gynaecological lesions such as cervical polyp and decubitus ulceration of prolapse. More recently consideration has been given to the endometrial pattern and particularly hyperplasia of the endometrium. But many of the authors have not excluded such possible modifying circumstances as the presence of fibroids, granulosa cell or other tumour of the ovary or a history of the administration of oestrogen.

Benthin (1928) found endometrial polypi in 24 per cent. of cases of post-menopausal bleeding due to benign conditions of the body of the uterus, but a description of the endometrial pattern is lacking. He considered that endometritis was an important factor in the other instances. The histological criteria for the diagnosis of "endometritis" are probably stricter at the present day and the diagnosis is less frequently

made. This observation is equally true of pre- and post-menopausal endometritis.

Schiffman (1929) likewise stressed the importance of endometrial polypi (11 out of 51 cases) but here again a histological description is lacking.

Fahmy (1933) in an analysis of results obtained by several observers on the subject of post-menopausal bleeding, grouped under the one heading such conditions as fibrosis uteri, ovarian dysfunction, metropathia haemorrhagica and endometrial hyperplasia. In many instances he recorded that the diagnosis was doubtful. Polyps are classified as benign tumours and no histological details are given. It is therefore impossible to assess the incidence of hyperplasia or other endometrial pattern in the cases he describes.

Geist and Matus (1933) recorded 182 cases of post-menopausal bleeding which they had personally investigated. They found polyps in 29 cases but did not differentiate between fibro adenomatous and cervical adenomatous varieties. Hyperplasia was present in 10 of their cases (1 adenomatous polyp being included) but in 3 cases fibroids of the uterus were also present. In 13 patients they

could find no cause for the complaint.

Breipohl (1935) who included patients within 6 months of the menopause found atrophy in 76 cases, hyperplasia in 13 and secretory endometrium in 3. For the purposes of this calculation he considered non-productive curettage of the uterus to represent atrophy.

Taylor and Millen (1938) analysed 406 cases of post-menopausal bleeding and after elimination of those with an obvious pathological lesion were left with 34 patients in whom bleeding occurred from a grossly normal uterus. Of this number, prolapse was present in 9 and endometritis in 6. The varying patterns of the endometrium are detailed in the 19 functional bleeding cases. Endometrial polyps were not considered as altered endometrial pattern but as benign growths.

Keene and Dunne (1938) in a series of 782 cases of post-menopausal bleeding found hyperplasia of the endometrium 13 times out of 38 cases in which no organic cause of the bleeding was demonstrable.

Te Linde (1940) contented himself with the statement that endometrial polyps occasionally

occur and it is impossible to assess endometrial patterns in his cases.

Novak and Richardson (1941) made a histological study of the endometrium obtained from women in the post-menopausal period. They made a serious attempt to analyse the endometrial patterns found, and as far as possible ruled out cases where there was an obvious source of bleeding such as carcinoma of cervix or cervical polyp. They did not exclude cases where small fibroids were present as they did not consider the presence of these benign tumours would influence the type of endometrium.

The percentage incidence of the patterns of endometrium found by them was:-

Atrophy	49.1 per cent.
Proliferative	16.9 per cent.
Hyperplasia	20.4 per cent.
Retrogressive	13.6 per cent.

For the purposes of comparison with Breipohl's figures it must be remembered that they ignored all cases where curettage did not produce sufficient endometrium for histological examination.

Geiger (1941) in an analysis of 395 cases of post-menopausal bleeding found 5 cases of endometrial

hyperplasia, an incidence of 1.2 per cent.

Schwartz (1943) did not differentiate clearly between hyperplasia and polypi, and a proportion of his cases had fibroids of the uterus present. Moreover it is doubtful if all the patients in his series had in fact had a complete cessation of menstruation. This probably accounts for the high incidence of secretory endometrium.

Cheek and Davis (1946) analysed 514 cases of post-menopausal bleeding. Details of the endometrial pattern are given in 38 cases where the bleeding could be termed functional; hyperplasia in 20 and polypi in 18. But the hyperplastic group included some examples of polypi, and there is therefore some uncertainty of the criteria of both polypi and hyperplasia. In six cases of their series endometritis was present.

Kottmeier (1947) described 148 cases of post-menopausal bleeding in which the endometrium showed signs of response to hormonal stimulation. In 30 cases they found an associated ovarian tumour and in 31 there was a history of the administration of oestrogen. Of the remaining 87 patients, 28 had bleeding within two years of the

menopause. They found an elevated urinary excretion of oestrogen in 65 patients and in 53 of these laparotomy was performed. A granulosa cell tumour was present 42 times. Of 90 patients with post-menopausal bleeding due to a uterine polyp in only two did an ovarian tumour develop.

Lund and Dougherty (1949) in a communication dealing with benign post-menopausal bleeding described the finding of active and "retrogressive" hyperplasia. They considered that the latter condition did not signify co-existing oestrogenic stimulation. Indeed they suggested that patients probably did not bleed from this condition and its finding was probably incidental.

Jones and Cantor (1951) dealt with functional bleeding of the post-menopausal epoch and distinguished between hyperplasia and polypi. They found endometrial polypi in 4 per cent. and hyperplasia in 3.6 per cent. of all cases. In discussing polypi they recorded their occurrence in uteri removed for other pathology.

It will be seen from this survey of the literature that it is difficult in the first instance to distinguish cases with organic lesions of the

genital tract from cases of functional post-menopausal bleeding. Moreover endometrial polyps are frequently mentioned but histological descriptions are lacking in most instances. With these reservations it is calculated that hyperplasia occurred 113 times in a total of 409 cases of functional post-menopausal bleeding. This represents an incidence of 28 per cent. Atrophy of the endometrium probably occurs in slightly over 55 per cent. of cases. Proliferative endometrium is mentioned only by a few authors but when it is assessed, it occurs in about 16 per cent. of the total of functional post-menopausal bleeding cases. Polypi and secretory endometrium make up the remainder but it is impossible to calculate the incidence with any degree of accuracy.

The incidence of active hyperplasia in functional post-menopausal bleeding in the present series is 20.5 per cent. compared with 1.7 per cent. in normal post-menopausal women. Moreover, proliferative endometrium represented 4.6 per cent. compared with 0.8 per cent. in the non-bleeding cases. Secretory endometrium which did not occur normally in post-menopausal women was found in

1.5 per cent. of cases of functional bleeding after the menopause. Thus in 26.6 per cent. of all cases of functional post-menopausal bleeding the endometrium showed histological evidence of activity. In 73.4 per cent. of these cases an inactive endometrium was present although a considerable proportion showed polypi or a diffuse cystic gland pattern.

In normal cases when hyperplasia was noted it occurred in the early years after the menopause. This suggests that it was in some way related to the endocrine imbalance known to be present around that period, and it is possible that in these cases the patient was still under the influence of the menopausal changes. Hyperplasia associated with bleeding, however, showed no particular age incidence in relation to the menopause. It was found from 1 to 34 years after the menopause and showed a fairly even distribution throughout the five-year age groups. It would appear therefore that hyperplasia in these circumstances is not a mere continuation of the changes which may be found at the menopausal period but is a new pathological entity.

Investigation of the menstrual history of these patients showed that there was no relationship between the occurrence of functional post-menopausal bleeding and any menstrual disturbance of the reproductive era. In addition in the few patients who had suffered from excessive bleeding before the menopause and who later complained of post-menopausal bleeding no correlation could be found between the endometrial patterns on these two occasions. For instance, hyperplasia associated with bleeding during the reproductive period was followed in 2 cases, 2 and 4 years after the menopause respectively by haemorrhage from an inactive gland pattern of the endometrium.

With the pronounced endocrine changes associated with pregnancy it might reasonably be expected that repeated pregnancies would have some influence on the character of the endometrium. It did not appear, however, that regeneration of the endometrium following labour or abortion influenced in any way the onset of bleeding or altered the endometrial pattern in these post-menopausal cases.

The striking feature of this group of cases

is the high incidence of hyperplasia and its occurrence many years after the menopause. This high incidence of hyperplasia is not unexpected since in the absence of demonstrble pathology, one would tend to assume that the symptoms are the result of endocrine influence. Although a number of factors may be responsible for maintaining the integrity of the endometrium the experimental work of Geist and Salmon(1941)would suggest that hyperplasia of the endometrium is particularly associated with oestrogen activity. This would provide a satisfactory explanation for the occurrence of hyperplasia in these cases of post-menopausal bleeding, and is supported by the occasional occurrence of a secretory endometrium, which was noted in 8 instances. Breophol reported 3 similar cases in a series of 130 patients with post-menopausal bleeding. Taylor and Millen also found a secretory pattern once in 34 cases of bleeding from a grossly normal uterus. Some objection may be raised to these reports since the authors state that in every instance the discovery was made within a year of the cessation of menstruation. In the present series a secretory pattern was found

from one to six years after the menopause.

Secretory activity in the endometrium during the reproductive life occurs under the influence of progesterone. It has been shown however that progesterone by itself is incapable of inducing such change unless the endometrium has been sensitised by oestrogen. It has, however, been suggested that a secretory endometrium may also result from the action of oestrogen and androgen the latter hormone being secreted by the theca cells of the ovary (Shippel, 1950). The occurrence of these cases thus strengthens the conception that post-menopausal bleeding is associated with some degree of oestrogen activity.

It must be remembered, however, that in more than 70 per cent. of the cases the endometrium was atrophic. This does not accord with the usual views relating to the effects of oestrogen activity on the endometrium. Two possible explanations arise for consideration. It may be that in these cases showing atrophy of the endometrium some agent other than oestrogen exists and is responsible for the bleeding. Alternatively it is conceivable that hyperplasia of the endometrium does not invariably follow upon oestrogenic stimulation.

For this reason it was decided to make a study of post-menopausal patients in whom an excess of oestrogen was presumed to be acting as in cases of granulosa cell tumours of the ovary. In addition patients known to be having oestrogen administered therapeutically were investigated with particular reference to the endometrial findings.

Group E

Over a period of twelve years eleven cases of granulosa cell tumour of the ovary have been found in post-menopausal patients in the Royal Samaritan Hospital for Women, Glasgow. A voluminous literature has accumulated relating to the condition. Novak and Brawner (1934); Bland and Goldstein (1935); Meigs (1935); Novak and Gray (1936); Pratt (1937); Chaney and Greenblatt (1938); Varangot (1938); Dockerty and MacCarty (1939); Dockerty and Counseller (1940); Karsner (1940); Traut and Marchetti (1940); Novak (1941); Henderson (1942); Novak (1942); Kottmeier (1944); Novak (1944); Hodgson, Dockerty and Massey (1945); Rhoads (1946); Dockerty (1947); Falls, Ragins and Goldberg (1949); Haines and Jackson (1950); Corscaden (1951); Diddle (1952).

There seems to be no doubt that these tumours secrete oestrogens as demonstrated by biological tests, (Frank, 1932; Gospe, 1936; and Palmer, 1939). For this reason these cases provide a control series whereby we may assess our findings in other groups. In view of the importance of this group, details of clinical history will be given for most of the cases.

CASE HISTORIES

Four of the cases had a typical history associated with a pelvic tumour and it was possible to make a presumptive diagnosis prior to operation, in two of them.

1. The first case was of an unmarried patient aged 67 who, 15 years after the menopause, began to have profuse vaginal bleeding. Five days after its onset she was admitted to hospital and curettage was performed. Examination at the time of the operation revealed the presence of a pelvic tumour. Histological examination of the endometrium showed active glandular hyperplasia. Laparotomy was performed a few days later and an inoperable ovarian tumour was found. Microscopical examination of a specimen showed it to be of the granulosa cell type.

2. A married patient aged 54 was admitted because of vaginal bleeding of 3 months duration occurring 4 years after the natural menopause. An ovarian cyst, the size of a melon, was discovered on abdominal examination. Hysterectomy and bilateral salpingo oophorectomy was performed. Naked eye examination showed a thickened endometrium.

Histological examination showed that the tumour was a granulosa cell carcinoma of the diffuse or parenchymatous variety and there was hyperplasia not only of the endometrium but also of the epithelium of the Fallopian Tube.

3. A woman aged 56 and 8 years after the menopause was admitted with a history of bleeding for three months. Curettage revealed a thickened endometrium which on microscopical examination was seen to be hyperplastic. At the time of operation an ovarian tumour the size of a tangerine was palpated on the right side of the pelvis. The association of these two findings led to a presumptive diagnosis of granulosa cell tumour. The diagnosis was confirmed when the ovarian tumour was subsequently removed.

4. A granulosa cell tumour was removed from a patient who had complained of post-menopausal bleeding. The uterus was not removed and there was no opportunity to examine the endometrium.

In the following four cases the true diagnosis was unsuspected initially and it was only when the symptoms recurred, in three cases after the patients had received a "menopausal dose" of X-rays that the presence of a granulosa cell tumour was considered.

5. A married woman of 59 was admitted to hospital because of four severe haemorrhages which had occurred in the previous 10 years. The patient had ceased to menstruate at the age of 40. Curettage revealed the presence of active hyperplasia of the endometrium and a "menopausal dose" of deep X-ray was given. Six months later because of bleeding of a fortnight's duration hysterectomy and bilateral salpingo oophorectomy was performed. The ovary contained a granulosa cell tumour and active hyperplasia of the endometrium was present.

6. A married woman 14 years after a natural menopause complained of bleeding of six months duration. Curettage produced bulky curettings which showed active hyperplasia. Three and a half years later there was a recurrence of bleeding and a further curettage was performed. Again the endometrium was thickened and on histological examination showed active hyperplasia. A small granulosa cell tumour of the ovary was found on laparotomy.

The true nature of the condition was not appreciated at the time hysterectomy was performed and it was only after histological examination that a diagnosis could be made in two cases.

7. A married patient of 56 complained of irregular bleeding for the previous 6 months. Bulky endometrium showing active hyperplasia was obtained on curettage. A "menopausal dose" of deep X-ray was given. There were recurrences of bleeding thereafter and one year later curettage was repeated. The cervix and vagina were noted to have the appearances seen in women of the reproductive phase of life and mucus was being secreted by the cervix. The endometrium was hyperplastic and it was considered advisable to perform a laparotomy. The ovaries were not noticeably enlarged but histological examination showed islands of granulosa cell tumour.

8. A nulliparous patient aged 60 was admitted to hospital because of vaginal bleeding occurring 8 years after the menopause. Curettage was performed and the endometrium showed cystic glandular hyperplasia of such a degree that it was reported as being obviously under the influence of oestrogen. There was, however, no history of the administration of oestrogen. Two years later the patient was readmitted to hospital having had bleeding comparable to a menstrual period at intervals from one to

four months. Curettage was again performed and bulky curettings obtained. Again the endometrium showed such active hyperplasia that it was suggested that it was being acted on by oestrogens. Hysterectomy and bilateral salpingo oophorectomy was performed but even at operation an abnormality of the ovary was not obvious. At pathological examination the left ovary was seen to be atrophic. The right ovary measured $\frac{3}{4}$" x $\frac{1}{2}$" and when it was bisected it was seen to contain a white tumour less than half an inch in diameter. Histological examination showed it to be of the granulosa cell type.

9. Case 9 is interesting in that the initial complaint of bleeding 20 years after the menopause did not recur after curettage. The patient aged 70 and was 20 years after the menopause when bleeding occurred. Post-menopausal hyperplasia of the endometrium was discovered. Six years later she was admitted to another hospital because of abdominal pain. At laparotomy an ovarian cyst which had undergone torsion was discovered. Histological examination showed it to be of the granulosa cell type and the endometrium showed active hyperplasia.

The following two cases are of importance because they provide material for discussion when considering the relationship of endometrial pattern to the occurrence of bleeding.

10. A married patient aged 59 and 19 years after the menopause was admitted because of four severe haemorrhages in the previous 10 years. Curettage revealed an inactive cystic glandular pattern of the endometrium. Deep X-ray therapy to the ovaries was given but six months later the patient was readmitted because of a recurrence of bleeding. Hysterectomy was performed. The endometrium lining the uterus showed an inactive cystic gland pattern and the ovary contained a granulosa cell tumour.

11. An unmarried patient aged 56 and 16 years after the menopause was admitted because of abdominal pain. There was no history of bleeding and a granulosa cell tumour of the ovary was found. The endometrium showed an inactive gland pattern.

It will be seen from the above that eight of these followed the usual clinical course of this condition. They are of considerable interest to the clinician in that it was possible to make the diagnosis of granulosa cell tumour even in the

absence of a palpable pelvic mass. This can be observed in cases 4, 5, 6 and 7. It would appear that bleeding with hyperplasia recurring after curettage in the post-menopausal patient and in the absence of any local pathological condition is probably due to granulosa cell tumour.

A "menopausal dose" of deep X-ray is frequently employed in the treatment of menopausal haemorrhagia and it would seem to result in cessation of ovarian function with subsequent cure of the abnormal bleeding. When the hyperplasia and bleeding occur in the post-menopausal epoch and are due to a granulosa cell tumour of the ovary, the bleeding shows a tendency to recur. This suggests that the ovarian tumour cells may have their function temporarily destroyed by the X-rays. The cells eventually recover their vitality and apparently the endocrine function is unimpaired. This is deduced from the recurrence of hyperplasia and bleeding in such cases.

It is noteworthy that in one case (No.9) curettage resulted in cessation of bleeding but hyperplasia persisted or recurred. From a study of normal post-menopausal women it is obvious that

hyperplasia may exist independently of the occurrence of bleeding and this case emphasises that finding. While there may be some inter-relationship it is not necessarily direct. This is also suggested by the findings in Case 10 in which bleeding was twice noted in association with an inactive gland pattern.

The finding of an inactive gland pattern without bleeding in association with a granulosa cell tumour is difficult to interpret. It may be that the tumour in this case had no functional activity in relation to endocrine production.

There are many references in the literature of the past 25 years to the occurrence of granulosa cell tumours and particular stress has been laid on the occurrence of hyperplasia of the endometrium in such cases. Novak and Brawner (1934) in a study of granulosa cell tumours found that of the six occurring in the post-menopausal age there was coincident hyperplasia of the endometrium in five. Henderson (1942) found hyperplasia of the endometrium (in one case associated with a polypus) in every post-menopausal case. Haines and Jackson (1950) reported on a series of granulosa cell tumours

including 19 cases occurring after the menopause. Only two thirds of the number actually suffered from post-menopausal bleeding. In the others the complaint was of pain in or swelling of the abdomen. The endometrial pattern was only noted in nine cases and in seven instances it was of the strongly oestrogenic type. They also refer to the finding of an endometrial polyp and in at least one case no endometrium was obtained at curettage. Spencer and Hollenbeck (1947) also report the presence of hyperplasia in two cases out of three. There was no bleeding in the other example. In a number of other cases the instance of hyperplasia is less convincing. Rhoads (1946) refers to the finding of mild physiological hyperplasia of the endometrium in association with a granulosa cell tumour of the ovary. Brewer and Jones (1933) in describing three cases obviously consider endometrial polypi as manifestations of hyperplasia. They describe polyp with spare narrow tubular glands and a dense stroma. Bianco and Favorite (1946) make the somewhat vague statement that in the case of granulosa cell tumour reported by them the endometrial picture was compatible with that

described by others in a similar condition.

Stohr (1942) found uterine bleeding with or without hyperplasia of the endometrium was present in 71.7 per cent. of cases of granulosa cell tumour of the ovary. In 28.3 per cent. there was failure to produce hyperplasia or bleeding but of these cases only two had occurred after the menopause.

Finally Diddle (1952) collected and analysed as many as possible of the recorded case reports of patients with granulosa cell tumours. Data concerning the endometrium was available in two thirds of all cases. There were 415 instances of hyperplasia as opposed to 25 of atrophic change. Endometrial polyps were seen more commonly in women with endometrial hyperplasia that in those without.

Interpretation

While there may be an occasional case in which the tumour is functionally inactive, the great majority of granulosa cell tumours do have an endocrine effect and it has been proved by Frank, Gospe and Palmer that they do produce oestrogen. Cases 9 and 10 are the most significant in relationship to this thesis in that bleeding and

hyperplasia are shown to be separate entities in these cases. Hyperplasia may occur in the absence of bleeding. This may well be related to particular oestrogen blood levels. At the same time it is even more interesting to note that bleeding may occur in the absence of hyperplasia. That bleeding per se in these cases is due to the action of the tumours is shown in Case 12 where removal of the tumour alone resulted in cessation of bleeding.

Experimental evidence is always more convincing than an uncontrolled natural phenomenon even when the changes are as striking as those presented by the above cases. It was therefore thought that valuable evidence might be obtained from a study of material obtained following the administration of oestrogens to patients. Before proceeding to this, however, the following case may prove of interest in that it provides further evidence, albeit indirect, for the presence of oestrogen activity in post-menopausal bleeding.

An unmarried nulliparous patient aged 65 years and 16 years past the menopause was admitted with a history of vaginal bleeding of a fortnights duration. Curettage was performed and active

hyperplasia of the endometrium was diagnosed. A week later hysterectomy was performed. The left ovary was enlarged to four times its normal size and contained a smallthecoma.

Bleeding in patients who have been receiving oestrogen therapy.

A number of writers have discussed the relationship between post-menopausal bleeding and oestrogen therapy and have condemned the indiscriminate use of oestrogens in post-menopausal patients, Novak (1944-a); Cheek and Davis (1945); Noyes (1945); Feeney (1947); and Kanter and Kawans (1950).

A history of administration of oestrogens either orally in the form of stilboestrol or by inunction of an ointment containing oestrogen was obtained in 29 cases of post-menopausal bleeding - an incidence of 1.4 per cent. It is probable that this figure errs on the low side as occasionally a patient may be having oestrogen therapy from her practitioner without being aware of the fact and without the practitioner making it known to the consultant. The commonest indications for the giving of oestrogen were kraurosis or the troublesome symptom of 'hot flushes'. But in a

proportion of cases the rationale was not clear, no gynaecological symptom being present. The patients' ages varied from 46 to 74 years and they were from 4 to 23 years past the menopause.

Even where a clear cut history is obtained that a patient suffering from post-menopausal bleeding has been receiving oestrogen, curettage is frequently performed to exclude a possible co-existing malignant condition. This precaution was taken in all the cases in this group in the present series, no endometrium being obtained in eight cases. Active hyperplasia of the endometrium was discovered eight times, atrophy six times, an inactive dilated gland pattern five times and proliferation of the endometrium twice. The incidence of an active endometrial pattern was therefore 34.5 per cent. in patients known to have received oestrogens prior to curettage.

It was not possible accurately to determine in all cases the amount of oestrogen administered nor the duration of the treatment, and I have not been able to correlate these factors with the endometrial pattern present. Two cases however, by reason of the contrast they provide, are worthy

of note. There was one instance of an extreme degree of active hyperplasia of the endometrium following the use of an ointment containing only a very small amount of oestrogen over a period of several weeks. By comparison, no endometrium was obtained on curettage from the uterus of a patient who had been taking stilboestrol daily over a period of two years.

The ability of oestrogen to produce hyperplasia of the post-menopausal endometrium is well established (Taylor 1932) and bleeding from the uterus after the administration of oestrogen is a clinical entity sufficiently common to have been termed "oestrogen-withdrawal" bleeding. The incidence of a history of the administration of oestrogen i cases of post-menopausal bleeding is variously reported at 2.3 per cent. (Cheek and Davis, 1946) to 4.5 per cent. (Jones and Cantor, 1951).

It has been considered that oestrogen produces hyperplasia of the endometrium and when the hormone is withdrawn, degeneration of the endometrium occurs with subsequent bleeding. Novak (1944-a) while not giving figures, states that the prevailing endometrial pattern in such cases is active hyper-

plasia. But he also describes cases in which a typical picture of "retrogressive hyperplasia", i.e. an inactive dilated gland pattern was seen.

Cheek and Davis (1945) recorded that in most of their cases relatively little endometrium was obtained, active hyperplasia being present in only two out of twelve instances. Geist and Salmon (1941) found a histological pattern of proliferation with distended glands, the endometrium later showing a quiescent state.

Thus it would seem that a known factor, i.e. oestrogen is involved and that bleeding in post-menopausal women follows the administration of this hormone. And as has been shown, there is a high incidence of active hyperplasia of the endometrium in these cases. But it is surprising to find bleeding without an endometrial pattern usually taken to indicate oestrogen activity. In considering the effect of endocrine action on any tissue the reactivity of the end organ concerned must be taken into account. Further evidence of the importance of this factor is afforded by the exceptional occurrence of hyperplasia of the breast tissue in elderly women following the administration

of oestrogen.

Summary

1. The pathological findings in 2056 cases of post-menopausal bleeding were analysed.
2. Eleven cases of granulosa cell tumour of the ovary and one thecoma were described.
3. Malignant conditions of the genital tract were responsible for the bleeding in 27.8 per cent. of the total cases.
4. In cases where a benign extra-uterine source of bleeding was present there was no significant variation in the incidence of endometrial patterns compared with the normal.
5. An increased incidence of hyperplasia was noted in cases of fibroids of the uterus.
6. Functional post-menopausal bleeding accounted for 26.1 per cent. of the total cases.
7. The incidence of hyperplasia in functional post-menopausal bleeding was 20.5 per cent.
8. Active hyperplasia associated with bleeding was not restricted to the early post-menopausal years, but typical examples occurred as late as 30 years after the cessation of menstruation.

9. Secretory endometrium was found in 1.5 per cent. of cases.

10. Infection of the endometrium occurred in 4.3 per cent. of cases of "functional" postmenopausal bleeding. Infection, both pyogenic and tuberculous, occurred not only in association with an inactive endometrium, but was found in cases of active endometrial hyperplasia.

11. Investigation of patients receiving oestrogen therapy revealed that bleeding due to this substance was not always associated with endometrial hyperplasia, only 34.5 per cent. showing an active endometrial pattern.

SECTION 3

SIGNIFICANCE OF SENILE ENDOMETRIAL POLYPI

There is frequent reference in the literature to the occurrence of endometrial polypi in normal post-menopausal women, in patients suffering from bleeding after the menopause and in association with endometrial carcinoma. Novak (1941) and Speert (1949) report this finding in normal post-menopausal women. The finding of such polyps in post-menopausal patients with bleeding is noted by Fahmy (1933), Te Linde (1940), Schwartz (1943) and Jones and Cantor (1951), and the association of endometrial polyps and carcinoma is referred to by Beattie (1933), and Hertig and Sommers (1949).

The term polyp is a clinical rather than a pathological one, referring simply to a growth which is attached by a pedicle, and not indicating in any way its histological characters. The endometrial polyp consists of a localised heaping up of that tissue. These polyps may be single or multiple, small or large enough to fill the uterine cavity. The pedicle may be short or so long that the body of the polyp protrudes the cervix.

During the reproductive life polyps may be functional and correspond to the general endometrial pattern. This is exemplified in cases of cystic glandular hyperplasia of the reproductive years where the whole of the endometrium lining the uterus is thickened and in areas it is polypoidal. In the post-menopausal woman, however, the polyp seems to bear little relationship to the endometrium lining the rest of the uterine cavity. The polyp is frequently solitary, composed of an inactive dilated gland pattern, and found in association with a thin or inactive endometrium. The essential difference between the two conditions is that whereas in hyperplasia the polyp is an integral part of a generally hyperplastic endometrium, in the post-menopausal era the polyp is the sole thickened portion of the endometrium lining the cavity.

It is obvious from a survey of the literature that there is considerable difference of opinion concerning the significance of these polyps and the mode of their development. In general their presence has been interpreted in four different ways.

Cheek and Davis (1946), Taylor (1932) and Schwartz (1943) although listing endometrial polypi and hyperplasia separately in their causes of post-menopausal bleeding nevertheless refer to the frequent finding of polypi associated with hyperplasia. This suggests a common aetiological factor and Taylor refers to the already recognised relationship which exists between the two conditions.

Novak and Richardson (1941) gave the name "retrogressive hyperplasia" to the inactive cystic gland pattern which is present in these polypi. They considered that these polypi occurred in patients whose terminal menstrual cycles had been anovulatory, the endometrium showing cystic glandular hyperplasia. In the post-menopausal years a process of mummification takes place and the inactive cystic gland pattern develops. Thus according to both these views endometrial polyps with cystic dilated glands are related to endometrial hyperplasia. In the one case the hyperplasia is thought to be co-existent and in the other preceding - often by many years - the formation of the endometrial polypi.

Other observors have not related the production of an endometrial polyp with hyperplasia, past or present. Fahmy (1933) and Taylor and Millen (1938) regard polypi of this nature as benign tumours. Lund and Dougherty (1949) refer to the confusion between hyperplasia and polyps. In their opinion, polyps are not related to generalised hyperplasia but the superficial histological similarity of the gland pattern may be responsible for an erroneous diagnosis of hyperplasia. Speert (1949) considers that the dilated glands of which these polypi are composed represent simple retention cysts, and the polyps themselves are merely a localised aggregation of such distended glands.

In the preceding sections of the thesis these polypi have been placed in a separate group, but in view of the suggested relationship between polypi and hyperplasia it is necessary to compare the incidence of the two conditions in the post-menopausal woman - with and without bleeding. In the following only polypi of an inactive type as described in the first section of the thesis are considered.

Patients Without Bleeding

Total number of cases	1520	
Cases of polypi	80	representing 5.2 per cent.
Cases of hyperplasia	26	representing 1.7 per cent.

These figures represent the findings on curettage and in the section of the thesis dealing with the normal post-menopausal endometrium arguments were adduced which suggested that the real incidence of polypi was considerably higher. When the entire uterus was available for study the incidence of polypi was 15 per cent. If the former figure is utilised the ratio between endometrial polypi is 3 to 1, or, if the more accurate figure is accepted the ratio becomes 8 to 1.

Patients With Bleeding

In cases of functional post-menopausal bleeding the incidence of endometrial polypi and hyperplasia is as follows:-

Total number of cases	537	
Cases of polypi	76	representing 14.1 per cent.
Cases of hyperplasia	110	representing 20.5 per cent.

The ratio between endometrial polypi and

hyperplasia is now reversed, being 2 to 3. If we accept the higher figure of 15 per cent. as the incidence of polypi in normal post-menopausal women, we find in the patients with bleeding that this is not materially altered from the normal figure.

This great diminution in the ratio of polypi to hyperplasia of the endometrium scarcely suggests that these focal lesions are examples of hyperplasia. It may be, however, that these polypi represent an example of previous hyperplasia which has undergone retrogression and one would naturally expect this feature to be related to a time factor. If this is so it ought to be apparent in an analysis of age groups. In the following table the total number of cases in all groups, normal and pathological, have been assessed according to the incidence of polypi and endometrial hyperplasia in the various post-menopausal age groups.

At first sight it may appear from Table 20 that there is an inverse relationship between hyperplasia and polypi but if the "under 5 year" group are omitted it will be seen that the

incidence of polypi does not alter significantly. The low incidence of polypi in the first stage group is entirely fallacious and is due to the marked variation in endometrial pattern at this time. It would appear from the figures that there is no statistical evidence to suggest that endometrial polypi are directly related to hyperplasia.

Table 20.

Time after menopause in relation to hyperplasia and endometrial polypi.

Years after the Menopause	Hyperplasia	Polypi
6 - 10	31.3	18.9
11 - 15	24	42.3
16 - 20	16.4	49.8
Over 20 years	18.0	50.3

A study of the histology of these endometrial polypi gives a general impression of inactivity of the tissues. The epithelium lining the glands is flattened and mitotic figures are absent. The stroma is less cellular than endometrial stroma usually is and mitotic figures which are so prominent in active hyperplasia are rarely present. Indeed the resemblance to hyperplasia is entirely based on the disparity in the size of the glands,

and it is noteworthy that the glands of polyps frequently attain a size much larger than is ever seen in active hyperplasia. This does not accord with the findings of Taylor, who in a study of 50 endometrial polyps found associated generalised mucosal hyperplasia in one third of 18 polyps. In addition, in 33 he found gland patterns essentially similar to that found in diffuse disease and which exhibited the same variations in degree of hyperplasia. Lund and Dougherty (1949), however, referred to the confusion between endometrial hyperplasia and polyps. They considered that polyps grew because of a local stimulation as distinguished from hyperplasia which had a more uniform generalised activity. Kottmeier (1947) described 148 cases of post-menopausal bleeding in which there was hyperplasia of the endometrium. In the majority of his cases there was either a history of administration of oestrogen (31 cases) or a granulosa or theca-cell tumour of the ovary was present (72 cases). By contrast, in 90 cases of bleeding due to an endometrial polyp in only two did an ovarian tumour develop. Thus neither Lund and Dougherty nor Kottmeier were of

the opinion that a polyp of inactive cystic gland pattern signified co-existing oestrogen stimulation.

In view of the suggestion that this gland pattern designated "retrogressive hyperplasia" by Novak is related to hyperplasia occurring at the time of the menopause a study of the age at menopause and type of menopause experienced was made. The average age at menopause was 47.8 years - a figure which is in close agreement with the average age in all the endometrial patterns studied. Patients in whom polypi occur do not have a later menopause then patients who later show endometrial atrophy.

There were 156 patients in whom endometrial polyp was noted. In 147 instances the menopause occurred naturally without excessive bleeding at that time. There were 3 cases where a menopausal dose of X-ray was given because of menopausal menorrhagia and twice radium was given for similar indications. There were 3 patients in whom the menopause followed bilateral oophorectomy undertaken because of benign ovarian cysts or salpingo oophoritis. Thus in only 5 cases out of 156 was there menopausal menorrhagia and in one of

these cystic glandular hyperplasia was present. Cystic glandular hyperplasia was also noted at curettage a year before the menopause in one instance. The periods subsequently were normal and X-ray treatment was not given.

The first patient at the age of 49 had suffered from irregular bleeding for six months. Curettage was performed and cystic glandular hyperplasia of the endometrium was diagnosed. Thereafter the periods were normal for 2 years at which time they stopped. After 18 months amenorrhoea she had further bleeding for a fortnight and was admitted to hospital for investigation. At operation she was found to have a senile vaginitis and on curettage an endometrial polyp was removed. On microscopical examination it was seen to be of the inactive type, with greatly distended glands.

The second patient also aged 49 had had prolonged and irregular periods for a year before her first admission to hospital. Curettage produced thickened endometrium showing the typical changes associated with metropathia haemorrhagica. A menopausal dose of deep X-ray was given, but the patient had further bleeding four months later.

Additional deep X-ray therapy was given. There was no further bleeding until four and a half years later. Although preliminary curettage revealed scanty endometrium hysterectomy was performed. When the uterus was opened an endometrial polyp, necrotic at the tip was discovered at the fundus. On histological examination it was seen to have distended glands lined by flattened epithelium and it was quite inactive in appearance.

These two cases represent the finding of a post-menopausal endometrial polyp in patients who were known to have had menopausal hyperplasia. But the fact that this sequence was only noted twice in 156 cases suggests that this is not in fact the normal mode of development of endometrial polyps.

Thus the diffuse gland pattern occurs normally in 20 per cent. of post-menopausal women and polyp formation of similar appearance was noted in an additional 15 per cent. If such patterns were to be considered the aftermath of hyperplasia at the time of the menopause as suggested by Novak and Yui the inference would be that such a condition was present in more than one

third of all women of this age. This does not seem likely from a clinical history of the patients with polypi and Sharman's (1953) findings suggest that ovulatory cycles rather than hyperplasia are the normal findings in the terminal menstrual cycle of women.

Indeed as has been stated the appearance of the histology of the polyps is one of inactivity. The epithelium of the glands is flattened and inactive differing from the atrophic pattern only in the flattening of the cells due to distension of the glands. The stromal cells likewise show lack of mitotic activity and are similar in appearance to those found in atrophic endometrium. In other words the only difference between an atrophic endometrium and the diffuse cystic glandular pattern is the presence in the latter of distended glands. These may well be simply retention cysts and in Speert's view they result from the occlusion of the gland openings which is caused by atrophy and contraction of the lining epithelium. Such an explanation is in accord with the frequency of occurrence of the dilated gland pattern which would imply a cause operative in

more than one third of cases. It is also compatible with the inactive appearance of the stroma.

The incidence of endometrial polypi throughout the post-menopausal years from 1 to 34 years after the menopause, does not suggest progressive growth such as might be expected if the polyp represented a benign tumour. Thus there is no evidence that endometrial polypi of inactive gland pattern are examples of active hyperplasia nor yet of retrogressive hyperplasia. Nor do they appear to be neoplastic in origin. Rather the diffuse cystic gland pattern is to be regarded as a variant of atrophic endometrium. And polypi would appear to be local aggregations of endometrium of cystic gland pattern.

SECTION 4

THE RELATIONSHIP OF ENDOMETRIAL HYPERPLASIA TO CARCINOMA.

In most cases of active hyperplasia of the post-menopausal endometrium the histological appearances are obviously benign. There are however a few instances in which the degree of activity is such that it may resemble actual adenocarcinoma. Novak and Rutledge (1948) have recently drawn attention to an atypical form of hyperplasia which may be confused with endometrial carcinoma. This group of cases is not large but the occasional resemblance in gland pattern between the two conditions has led to the suggestion that they are both the result of the same stimulus. If this were so it might be that hyperplasia was a precursor of endometrial carcinoma, a relationship analogous to that said to exist between cystic dysplasia and carcinoma of the breast. From this it has been argued that the stimulus responsible for the development of hyperplasia, if allowed to act for a sufficiently long time, might produce malignant change in the endometrium in susceptible women.

I do not propose to consider the problem of the aetiology of carcinoma of the endometrium except in relation to post-menopausal hyperplasia of the endometrium. Much of the literature deals with the role of hyperplasia of the endometrium during the reproductive life or near the menopause. But hyperplasia of the reproductive era is a reversible process and thus differs from the condition as it is found after the menopause.

It has been shown that functional disturbance of the uterus in the post-menopausal phase is associated with a marked increase in the incidence of endometrial hyperplasia. A study of patients with granulosa cell tumours of the ovary and of post-menopausal women receiving oestrogen therapy has indicated that the changes found in patients suffering from functional haemorrhage may also be related to oestrogens. This suggests several possible lines of investigation into the problem of the relationship of endometrial hyperplasia to carcinoma. A number of authors have tried to relate the type of endometrium existing in the post-menopausal period to the subsequent development of carcinoma. Hertig and Sommers

(1949) reported the finding of endometrial hyperplasia in a number of cases where curettage had been performed a number of years prior to the discovery of carcinoma. Burch (1934) on the other hand states that he has never observed hyperplasia associated with or as forerunner of carcinoma of the endometrium. Indirect evidence of a hyperplastic process, probably related to oestrogen stimulation has been reported by Ayre and Bauld (1946) who studied the changes in vaginal smears in cases of uterine carcinoma. As a result of clinical investigations Randall (1945) states that adenocarcinoma does not occur in the uterus of a woman whose vulval and vaginal tissues suggest deprivation of oestrogenic hormone.

There are several possible lines of investigation of any relationship between endometrial hyperplasia and the development of carcinoma. In the first place examination of material from cases of endometrial carcinoma ought to show a high incidence of hyperplasia in the uninvolved endometrium. Although this has been attempted by other writers it is necessary to point out that hitherto the normal post-menopausal endometrial

patterns have not been taken into consideration when assessing results. Secondly, if cases of post-menopausal endometrial hyperplasia are studied over a period of years one would expect to find the incidence of carcinoma to be greater in this group than in the general female population. And pursuing this argument in the opposite direction, investigation into the type of endometrium known to have been present prior to the development of endometrial carcinoma should show a high incidence of hyperplasia.

Although it has been shown in a previous section of the thesis that senile polypi are unlikely to be an expression of hyperplasia, nevertheless their possible relationship to endometrial carcinoma must be considered particularily since a number of authors regard them as benign tumours.

Hyperplasia preceeding carcinoma.

It has been shown in a previous section of the thesis that it is not normal for active hyperplasia of the endometrium to be present in the post-menopausal woman without producing symptoms, particularly haemorrhage. It therefore

seems reasonable to expect that, if endometrial carcinoma is in fact preceeded by post-menopausal hyperplasia, most patients would have a history of long continued intermittent bleeding. 116 cases of endometrial carcinoma in post-menopausal women were analysed in relation to the duration of bleeding before the discovery of carcinoma.

Table 21

Duration of bleeding in cases of endometrial carcinoma.

Duration of Bleeding.	No. of Cases	Percentage
Under 6 months	60	51.7
6 months - 1 year	34	29.3
1 year - 3 years	20	17.2
Over 3 years	2	1.7

It will be seen from the above table that in more than half the cases bleeding had been present for less than six months before curettage revealed the presence of carcinoma of the endometrium. In several cases the duration of bleeding before the diagnosis was made was less than a week. In 80 per cent. of the total less than one year had elapsed from the onset of bleeding until gynaecological investigation was carried out.

There were only two cases in which bleeding

had occurred more than three years prior to the diagnosis of endometrial carcinoma. In both of these cases curettage because of bleeding had been performed and active hyperplasia was diagnosed.

It was thus quite common to find that a woman some years after the menopause developed bleeding, and when curettage was performed a few weeks later endometrial carcinoma was found.

If endometrial carcinoma is occurring in the same group of patients who have endometrial hyperplasia then one would expect that the tumour would develop in patients in an age group in reasonably close proximity to that in which hyperplasia is most frequently found. An analysis of patients with functional bleeding associated with hyperplasia relative to the time after the menopause when the bleeding occurs is shown in Table 22.

Table 22.

Time after the menopause of bleeding in cases of endometrial hyperplasia.

Years after the Menopause.	No. of Cases.	Percentage.
Under 5 years	50	45.5
6 - 10	23	20.9
11 - 15	18	16.3
16 - 20	9	8.2
Over 20 years	10	9.1

A similar analysis of cases of endometrial carcinoma is shown in Table 23.

Table 23.

Time after the menopause of bleeding due to carcinoma.

Years after the Menopause.	No. of Cases	Percentage
Under 5 years	29	25
6 - 10	32	27.6
11 - 15	15	12.9
16 - 20	17	14.7
Over 20 years	23	19.8

Bleeding occurred from 3 to 44 years after the date of the last menstrual period.

It is not essential that the stimulus responsible for the original development of endometrial carcinoma should persist for an indefinite period. In fact it need not necessarily be present at the time of the discovery of the carcinoma. It would be more logical to look for the stimulus or for the forerunner of carcinoma some years before the development of malignancy. In a consideration of the role of endometrial hyperplasia in the production of carcinoma findings at a prior curettage in the post-menopausal era would be of value.

A study of the literature shows that in this connection as in others most of the reports of hyperplasia refer to patients in the reproductive era and some to patients not long past puberty (Shaw 1929, and Hirst 1929). Where post-menopausal patients only are considered the number of cases is relatively small. Finding of hyperplasia prior to the discovery of endometrial carcinoma is reported by Morrin and Max (1939), Horsley (1924), Speert and Peightal (1949) and Hertig and Sommers (1949). On the other hand Burch (1934) and Taylor (1932) did not find any case in a post-menopausal women where endometrial cancer had definitely been preceeded by hyperplasia as established by curettage.

An investigation of 116 cases of endometrial carcinoma showed that in only 4 instances had a curettage been performed in the post-menopausal period before the diagnosis of malignancy was made. In 2 patients active hyperplasia of the endometrium was discovered 7 years and 6 years respectively before carcinoma was found. In neither case was X-ray treatment given after the original diagnosis of hyperplasia was made. The endometrial pattern

in both cases was quite obviously benign at the time of the first curettage. This finding is illustrated in Figure 4. In one other instance curettage, 2 years before the discovery of carcinoma, did not produce any endometrium for examination. In the remaining case prior curettage revealed an inactive glandular pattern in a polyp. This finding was made 18 years before the discovery of carcinoma. In half the cases of endometrial carcinoma in which a previous curettage had been performed in the post-menopausal period, hyperplasia was present at this time. Under four per cent. of the total cases of carcinoma, however, had had symptoms necessitating curettage. If it is accepted that patients without bleeding did not have hyperplasia of the endometrium, then the incidence of hyperplasia as a precursor of endometrial carcinoma is less than two per cent. This finding is in agreement with other reported series. Morrin (1944) described 4 such cases and Horsley (1924) reported one case but the original curettage at which hyperplasia was diagnosed was performed only 3 months before carcinoma was discovered. It is likely that the

explanation in this case is provided by Taylor's experience. He found 2 cases of adenocarcinoma where hyperplasia had been diagnosed at a previous curettage. Further study of the original sections however showed that the carcinoma had in actual fact been present at the time of the first operation.

Further examples of hyperplasia proceeding carcinoma are reported by Corscaden, Fertig and Gusberg (1946) - 5 cases and Speert and Peightal (1949) 6 cases. The most detailed paper is by Hertig and Sommers (1949). They were able to examine the endometrium in 32 cases of endometrial carcinoma. When the original curettage was performed 15 or more years prior to the development of cancer they found no endometrial abnormality. Seven cases fell into this category. Active cystic hyperplasia which occurred 17 times, was found mainly in the 6 - 13 year period before cancer developed. Adenomatous hyperplasia of which there were 19 examples was noted for the most part when the original curettage had been performed within 5 years of the development of endometrial carcinoma. They observed innocent polyp formation in 10 instances. It should be borne in mind however that 12 of 32 patients were

under the age of 45 years and it seems probable that a further number had not yet reached the menopause since the authors refer to the fact that they observed a decline of ovulatory cycles in patients between 40 and 50 years of age. Burch (1934) remained adamant that he has never observed hyperplasia as a forerunner to endometrial carcinoma.

Thus in all the literature there would not appear to be more than 30 authentic cases of post-menopausal hyperplasia as a forerunner of endometrial carcinoma. While previous curettage could only be studied in four cases of the present series, the very fact that the number exhibiting symptoms and requiring operative interference was so small indicates a certain measure of agreement with the above. If hyperplasia were an important factor in the development of carcinoma the incidence in previous curettage would be much more striking.

Follow-up of patients with endometrial hyperplasia.

An alternative method of studying this problem was to follow the history of patients known to have hyperplasia of the endometrium. It would seem that if endometrial hyperplasia was a frequent precursor of carcinoma then such an investigation would result in the finding of the development of

carcinoma in a proportion of such patients. It was decided to include only these patients whose history could be followed for a considerable number of years. No patients were included in which the period of follow-up was less than six years and the longest period of observation of a patient was 12 years. If carcinoma were to develop following hyperplasia in the post-menopausal era then it is likely that it would be observed in such a period of time.

Fifty eight patients were included in this series, and six of them could not be questioned, three having died of intercurrent disease and in three instances it was impossible to trace the patient. Three patients had been treated by hysterectomy and are also excluded from the analysis.

Of the 49 cases, 35 had been treated by curettage alone. There had been no further bleeding since operation in 26 of these patients. The remaining nine patients had a recurrence of bleeding and were subjected to curettage. In three cases curettage did not reveal the presence of any endometrium and since that time the patients

have had no further bleeding. The intervals between the finding of active hyperplasia and the non-productive curettage were 6 months, 2 years and 5 years respectively. There were four patients in whom bleeding recurred and in whose endometrium active hyperplasia was noted on both occasions. The intervals between the curettages were 3 years in 2 cases and 5 years in the other two.

One patient had a laparatomy performed after the second curettage and a granulosa cell tumour of the ovary was found. The second patient was aged 75 years and was 25 years after the menopause when bleeding was first noticed. At the second curettage there was extreme hyperplasia of the endometrium but there was no suggestion of malignancy. The vaginal lining was thick and rugose and the cervix was secreting mucus. All the evidence pointed to the fact that the patient's genital tract was under the influence of oestrogens and one's experience of similar cases suggested that there was in all probability a granulosa cell tumour of the ovary. The patient, however, was now 80 years old and laparotomy was not performed.

In the remaining two cases endometrial carcinoma

was found three years and seven years after the prior curettage at which hyperplasia was diagnosed. Search was made in further sections from the original blocks but no evidence of carcinoma was found in the earlier specimens.

There were nine cases in which a "menopausal dose" of X-rays was given to the ovaries after a diagnosis of post-menopausal hyperplasia of the endometrium had been established. Eight of these patients remained symptom free but the remaining patient had a recurrence of bleeding seven years afterwards. Curettage was performed and thickened endometrium was obtained. Histological examination revealed an inactive cystic glandular pattern of the endometrium.

In five cases active hyperplasia of the endometrium, discovered in the post-menopausal period, was treated by intra-uterine radium, the dosage ranging from 1,800 to 2,000 milligrammes - hours. Four of the patients had no further bleeding but in the remaining instance a recurrence of bleeding was noted three years later. Diagnostic curettage did not produce any endometrium for histological examination.

Thus 49 patients known to have had post-menopausal bleeding associated with active hyperplasia of the endometrium were observed for periods of from 6 to 12 years. Recurrence of bleeding occurred in eleven patients. In four cases no endometrium was obtained when subsequent curettage was performed. An inactive gland pattern was present in one instance. There were four examples of active hyperplasia, in one patient laparotomy revealed a granulosa cell tumour. There was strong presumptive evidence of a similar tumour in one other patient but her general condition was unsatisfactory and laparotomy was not undertaken. There were two instances of the development of endometrial carcinoma in patients who were known to have had post-menopausal bleeding some years previously and where endometrial hyperplasia had been diagnosed. Hintze (1929) in a follow-up of 24 cases of post-menopausal endometrial hyperplasia associated with bleeding did not find any evidence of carcinoma. The original treatment of the above patients had consisted solely of dilatation and curettage.

Vaczy (1948) found 8 cases of endometrial

carcinoma in a follow-up study of 520 cases of active hyperplasia. Not all of the patients were post-menopausal but the eight cases occurred in patients aged 40-60 years among 364 patients in that age group, an incidence of 2.1 per cent. The duration of observation of these patients was from five to fifteen years. Payne (1937) considered that the absence of bleeding for from one to twelve years warranted the assumption that malignancy had not developed. Winter (1950) in a study of 763 cases of active hyperplasia found seven cases of endometrial carcinoma an incidence of 1.44 per cent. He could not find any example of transition from endometrial hyperplasia to carcinoma. The incidence in the present series is 4.1 per cent. This is a higher incidence than that noted previously by other authors and might suggest some relationship between post-menopausal hyperplasia of the endometrium and carcinoma. It is probable however that the reason for the higher figure obtained in this series lies in the fact that a smaller number of cases was investigated. Moreover all the patients in the present investigation had experienced a definite menopause

with amenorrhoea for at least a year before the recurrence of bleeding associated with endometrial hyperplasia. Nevertheless even if the above figure of 4.1 per cent. is correct it provides no evidence for any close relationship between endometrial hyperplasia and carcinoma. The incidence of carcinoma of the corpus uteri in cases of post-menopausal bleeding from whatever source is 8.9 per cent. If endometrial hyperplasia was an aetiological factor in the causation of carcinoma one would expect that in any considerable series of cases of post-menopausal bleeding due to hyperplasia one would not expect the subsequent development of carcinoma to be 4.1 per cent. of cases, that is, less than half the general incidence in all cases of post-menopausal bleeding. On the contrary one would expect the figure to be much higher than that found in cases of post-menopausal bleeding irrespective of the cause, namely 8.9 per cent.

Hyperplasia in association with carcinoma.

In the early stages endometrial carcinoma is usually localised to a small area of the lining of the uterus. The rest of the endometrium is commonly involved at a rate which depends upon the

degree of malignancy of the tumour. There are many cases of adenocarcinoma however in which the gross lesion seems definitely circumscribed involving only a small area of the endometrial surface. In this group must be included a number of cases in which the carcinoma begins in the form of a localised polypoid growth in same portion of the uterine cavity. A study of the uninvolved endometrium would give information about the endometrial pattern found in association with endometrial carcinoma.

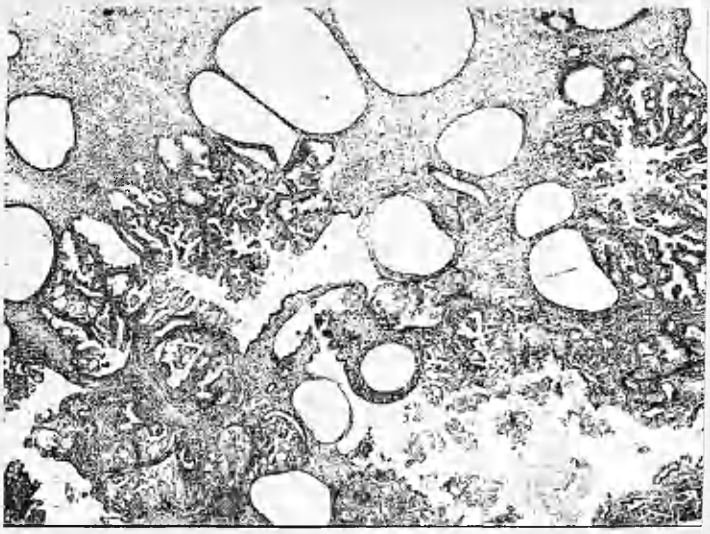
The literature contains many references to cases in which endometrial hyperplasia was found simultaneously with adenocarcinoma. A critical study makes it clear that in the majority of cases both hyperplasia and carcinoma occurred during the reproductive life of the woman or actually at the time of the menopause. Indeed in some instances the hyperplasia was diagnosed not long after puberty (Jones and Brewer, 1941; Hirst, 1929; Mazzola, 1938). The number of cases reported in which carcinoma was associated with hyperplastic changes in the uninvolved endometrium after a definite cessation of menstruation is much smaller

(Myer, 1922; Taylor, 1932; Novak and Yui, 1936 and Herrell, 1939). Similar studies by a number of investigators have led to directly opposite results (Cullen, 1900; Heurlin, 1911; Fluhman and Stephenson, 1929; and Fahlund and Broders, 1941).

Study of the uninvolved endometrium was possible in 56 out of 116 cases of endometrial carcinoma. In a number of cases the diagnosis was made from a study of curettings but for the most part the uninvolved endometrium was found in hysterectomy specimens. In 26 cases a cystic gland pattern was found and in 10 instances this took the form of a solitary polyp. There were 24 instances where the associated endometrium was noted to be atrophic. In five occasions (8.9 per cent. of the total) the association of endometrial hyperplasia and carcinoma was encountered. In the remaining instance a fibro adenomatous polyp was present in the endometrial cavity.

The association of the inactive gland pattern with endometrial carcinoma is well illustrated in Fig. 12. Fig. 13 and 14 are taken from a hysterectomy specimen.

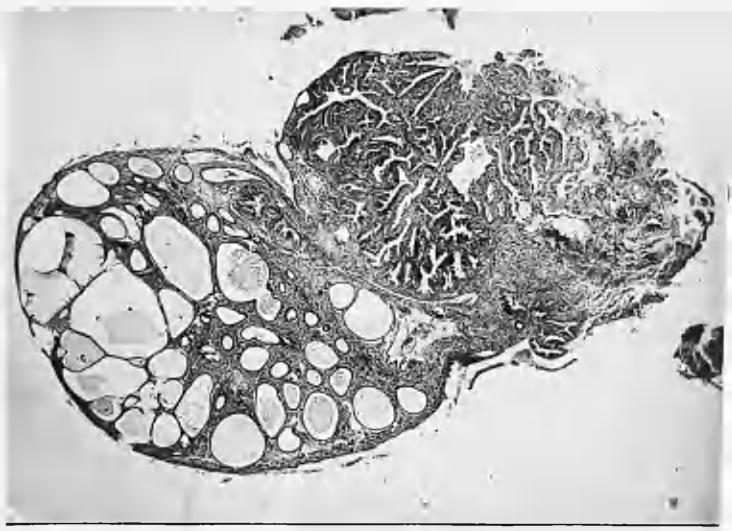
Figure 11.



Endometrial carcinoma associated with inactive dilated gland pattern - diffuse.

H & E x 30

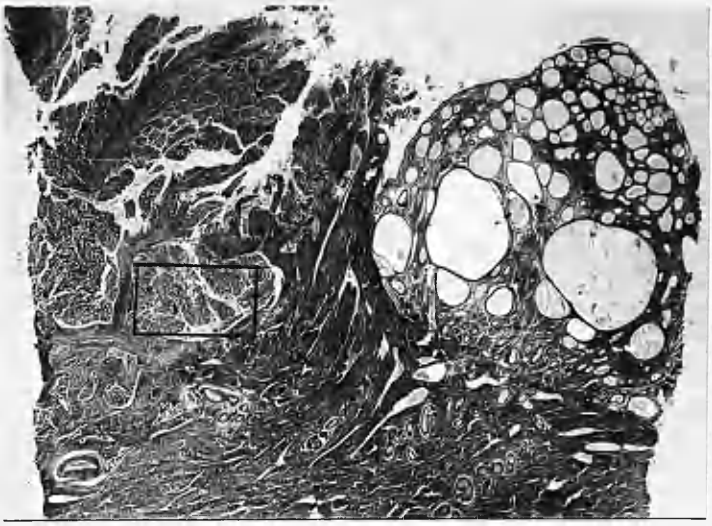
Figure 12.



Endometrial carcinoma associated with senile polyp of similar histological pattern to above.

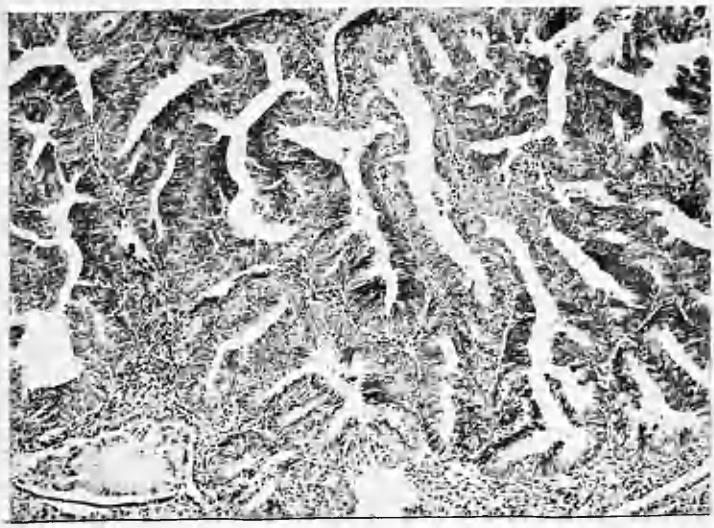
H & E x 15

Figure 13.



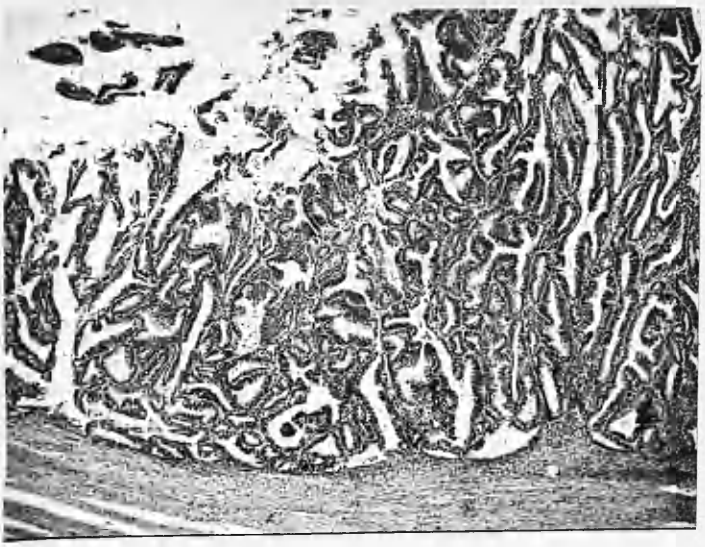
Endometrial carcinoma associated with senile polyp - hysterectomy specimen.
H & E x 4.

Figure 14.



Endometrial carcinoma - area indicated in Fig. 13 under higher power magnification.
H & E x 75.

Figure 15.



Endometrial carcinoma.

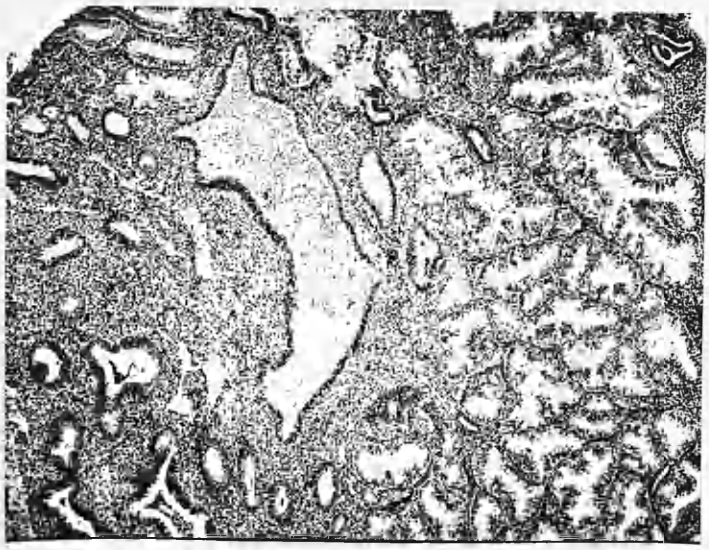
H & E x 60

Figure 16.

Uninvolved endometrium from the same case, showing atrophic features.

H & E x 60

Figure 17.



Endometrial carcinoma in association with cystic glandular hyperplasia.

H & E x 75

Meyer (1922) was the first to describe the occurrence of islands of cancer in areas of hyperplasia in four cases and the description follows closely the appearance in three of the five cases in the present series. Novak and Yui (1936) in a study of the uninvolved endometrium found it to be hyperplastic in no less than 40 per cent. of cases. This represents an incidence almost five times greater than that found in the cases I have studied. The diagnosis of hyperplasia in their cases was based on the finding of a "Swiss-cheese" pattern of the glands. In the discussion following the paper this interpretation of hyperplasia was criticised by Te Linde and Healy who suggested that many of the specimens designated hyperplasia were in fact inactive. Certainly some of the microphotographs illustrating this point show cystic dilated glands of an inactive type. Taylor (1932), reported four cases of endometrial carcinoma in postmenopausal women found in association with "proliferative" changes in the endometrium. In two of these cases, however, he refers to the numerous, very thin walled cystic glands which very strongly

suggests that these represent the inactive cystic pattern referred to above.

Payne (1937) found the association of hyperplasia and carcinoma five times as often in the post-menopausal as in the pre-menopausal group, but the same criticism applies to his criteria for the diagnosis of endometrial hyperplasia. It would seem that the gland size per se was adopted as a criterion in the diagnosis of hyperplasia of the endometrium. The histological appearance of inactivity in the gland and stroma cells was apparently overlooked. The crux of the matter is the significance to be attached to the cystic dilated gland pattern.

Fahlund and Broders (1941) and Heurlin (1911) found the uninvolved endometrium to be atrophic. Jones and Brewer (1941) found no evidence of oestrogenic stimulation of the endometrium in similar cases but in a number of their cases they observed a proportion of cystic dilated glands. The association of hyperplasia and carcinoma was noted only once in 23 cases of endometrial carcinoma by Fluhman and Stephenson (1929) an incidence approximately the same as in the present series.

Thus it would appear that the endometrium found in association with endometrial carcinoma in the post-menopausal woman is in 90 per cent. of cases atrophic, with cystic dilated glands in approximately half the cases. In less than 10 per cent. of cases was hyperplasia of the uninvolved endometrium found.

In addition it was shown in the section dealing with hyperplasia that there was no statistical relationship between hyperplasia and the inactive gland pattern. It is apparent from the description given by the various authors that the inactive gland pattern is assumed to be an example of hyperplasia, a supposition which has been shown to be quite unfounded. It has been shown in a previous section of the thesis that this pattern normally occurs in 35 per cent. of normal post-menopausal women. This fact has not been considered by the authors mentioned above and would appear to be the cause of the discrepancy in the findings reported.

Relationship between endometrial polypi and carcinoma.

The post-menopausal endometrial pattern found prior to the development of or in association

with endometrial carcinoma has been considered in considerable detail particularily in regard to the part played by hyperplasia. The possible relationship between carcinoma and endometrial polypi has not so far been dealt with specifically. It has been shown in a previous section of the thesis that there is no apparent relationship between the occurrence of polypi and hyperplasia. In all cases the polypi were found in association with an otherwise atrophic or inactive endometrium.

A number of authors have suggested that carcinoma may develop from endometrial polypi. Beattie (1933) in a study of 50 cases of carcinoma found two cases (four per cent.) of associated endometrial polypi. According to Stacey (1925) five per cent. of patients suffering from endometrial carcinoma had previously had polypi removed. In his article however he does not distinguish between endometrial and cervical polypi and it is impossible to assess the true incidence of the former. Hertig and Sommers (1949) however, in a study of curettings obtained from post-menopausal patients prior to the development of carcinoma found polypi in 10 out of 32 cases,

a remarkable incidence of 31.2 per cent. Moreover they noted endometrial polypi accompanied 46 (12 per cent.) of 389 cases of carcinoma. Taylor (1932) from a study of cases of carcinoma also came to the conclusion that polypi were an aetiological factor. The majority of his cases were in the reproductive phase of life and therefore not comparable with the present series.

It has been stressed in this thesis that the general term polyp is a clinical one rather than a pathological one indicating a certain histological structure. It is therefore necessary to qualify the term by indicating the pattern of glands and stroma and the degree of activity present. The fact that this has not been done in the above reports on this subject makes the interpretation of their findings difficult.

It has been shown that endometrial polypi are local aggregation of endometrial tissue and there is no evidence to suggest that senile polypi are neoplastic nor that they are related to endometrial hyperplasia. It does not appear therefore that it would be necessary or helpful to assess their significance in the development of

endometrial carcinoma apart from a consideration of the general endometrial pattern. This problem has been studied in the previous sections of the thesis. It is more important in this connection that the frequent occurrence of such senile endometrial polypi in normal post-menopausal women without bleeding is taken into account.

Relationship of oestrogen therapy to development of endometrial carcinoma.

Closely associated with the question of hyperplasia and its possible relationship to endometrial carcinoma is the problem of oestrogenic activity in such cases. Although no direct evidence has been brought forward, the various authors quoted have implied that the development of endometrial carcinoma is closely related to the continuous action of oestrogen. In this connection the close association between the chemical formulae of naturally-occurring oestrogens and known carcinogenic compounds may be significant. And apart from the aetiological significance it is a matter of profound clinical interest that long continued administration of oestrogen might cause the development of endometrial carcinoma. But as has been indicated previously there has been no convincing evidence that hyperplasia of the post-

menopausal endometrium and carcinoma are closely associated.

Cases of atypical hyperplasia of the endometrium strongly suggesting carcinoma in women who have been under treatment by oestrogens for long periods of time have been reported by Geist, Walker and Salmon (1941), Henry (1945) and Clemensen (1948). Nine cases of actual endometrial cancer have also been reported but the direct relationship between cause and effect is not of course established. In addition in many of the cases reported the patient had shown definite evidence of endocrine upset prior to the administration of oestrogen. Henry (1945) described an example of a patient who at the age of 46 had received a menopausal dose of deep X-ray because of menorrhagia. Curettage was not, however, performed at this time so the possibility that the carcinoma, which developed subsequent to oestrogen therapy, may have already been present at this time cannot be ignored. The case reported by Freemont-Smith, Meigs, Graham and Gilbert (1946), was of a patient who had many episodes of secondary amenorrhoea while still in her thirties.. Treatment with Stilboestrol was begun long before the

menopause and a causal relationship to the development of endometrial carcinoma is not established. Gusberg (1947) reported five cases but in three of them there was evidence of functional gynaecological disorder, as shown by irregular bleeding, prior to the administration of oestrogen.

I have not found a history of prolonged administration of oestrogen in any of the 116 cases of endometrial carcinoma. The only patient in this review who has had such prolonged oestrogen therapy had been receiving five milligrammes of Stilboestrol daily for two years. The endometrium showed active cystic glandular hyperplasia, the cervix was secreting actively and there was pronounced cornification of the superficial vaginal cells. The histological picture was, however, quite innocent.

Thus the total number of reported cases in this category is small compared with the amount of oestrogens administered to patients of this age group. It must be observed that, because of experience of bleeding associated with oestrogen therapy in the post-menopausal women, prolonged, uninterrupted administration of oestrogen is not

now commonly practised. Geist (1935) states that he has found no evidence to justify the fear that carcinoma of the endometrium might result from therapeutic use of oestrogen. Zondek (1947) has reported that during twenty years clinical experience with oestrogenic hormone he has not observed an instance in which the hormone had produced a malignant tumour. This view is shared by Greenblatt and Kuppermann (1947) who considered that the evidence of a carcinogenic activity of oestrogens in the human female was vague and at times only suggestive. Novak (1944) who is a protagonist of the theory that post-menopausal hyperplasia of the endometrium is a precursor of carcinoma, gave as his opinion that no case of human cancer has been recorded in which the evidence that oestrogen was responsible is unimpeachable. It is likely that some confusion of ideas has arisen due to the assumption that endometrial hyperplasia and oestrogen activity are synonymous. In a previous section of the thesis it has been shown that oestrogen therapy in the post-menopausal period causes hyperplasia in only 34.5 per cent. of cases.

Oestrogen activity in cases of endometrial carcinoma.

Attempts have been made to estimate the amounts of urinary oestrogen in cases of endometrial carcinoma. Herrell (1939) reported the isolation of 5 rat units of oestrin in twenty-four hour specimens in eight out of ten post-menopausal women with adeno-carcinoma of the uterus. Such quantities of oestrin however are similar to those found in the urine of normal male and female castrated patients, (Frank, Goldberger and Salmon, 1936). It is doubtful if these figures can be considered to be accurate. The biological methods of assay are at the best a rough assessment of the amount of oestrogen present and no reliable chemical method has been evolved. The method described by Tomnsett (1950) which depends upon a colorimetric reading was not found to be at all reliable in dealing with the small amounts of oestrogen involved in assay in patients past the menopause.

There is no convincing evidence that hyperplasia and endometrial carcinoma are associated and it has been shown that administration of oestrogen does not necessarily result in hyperplasia of the endometrium. It is therefore necessary to adopt some other technique which

might provide further evidence of oestrogenic activity. For this reason vaginal smears were examined from cases of endometrial carcinoma. This test is based upon the fact that the proliferation of the vaginal epithelium is dependent upon the ovarian hormones, particularly the oestrogens. The decline in ovarian function which occurs in the menopausal years thereafter leads to progressive thinning of the vaginal epithelium until finally in the post-menopausal years and in old age, progressive atrophy to even a single layer of cells may occur. Where marked oestrogen deficiency is present all the cells are from the basal layer of the vaginal wall. Leucocytes are numerous. Slight oestrogen effect is evidenced by the presence of cells from the superficial vaginal layer, the cytoplasm of the cells being basophilic. When there is a moderate to marked oestrogen effect the cells become acidophilic and cornification is sometimes present. High cornification is suggestive of disordered oestrogenic activity in a patient of the post-menopausal years, and is sometimes associated with endometrial hyperplasia.

Method

Preparation of Vaginal Smear.

The patient should not douche for at least 24 hours before the smear is to be taken. A glass pipette is introduced into the posterior fornix of the vagina, and the vaginal secretion is sucked in. The material is expelled on the surface of a clean slide and before the smear can dry it is fixed in equal parts of 95 per cent. alcohol and ether.

Staining Vaginal Smears.

The Shorr stain has the following formula -

Bielrich Scarlet (Water solution)	0.5 gm.
Orange G.	0.25 gm.
Fast Green F.C.F.	0.075 gm.
Aniline Blue (Water solution)	0.04 gm.
Phosphotungstic & Phosphomolybdic acid	0.5 gm.
Glacial Acetic Acid	1.0 cc.
Dissolve all completely in 50 per cent. ethyl alcohol.	100 cc.

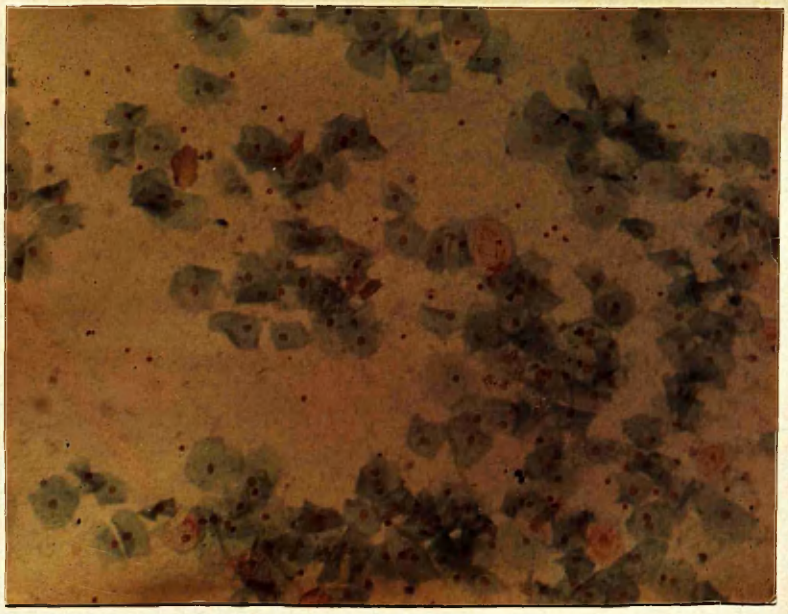
Ayre and Bauld (1946) and Docherty and Massey (1945) have found that vaginal smears of women with proved malignant disease of the corpus of the uterus showed evidence of high activity of endogenous oestrogen.

Vaginal smears were obtained from 32 patients known to have endometrial carcinoma. Slight oestrogen effect was found in 12 cases and oestrogen deficiency was present on 17 occasions. Moderate oestrogen effect was noted 3 times but there was not a single instance in which the oestrogen effect could be termed "marked". In no case was there cornification of the cells comparable to that found in patients known to be receiving oestrogen therapy or in a patient who had a granulosa cell tumour of the ovary. See Figs. 18 and 19.

These findings are contrary to previous reports.

It is possible to study this problem on a purely clinical basis. In the absence of oestrogens the vaginal tissues undergo atrophy and in a number of instances the degeneration of the tissues proceeds to a point where the condition merits the term of atrophic vaginitis. If increase of oestrogens is an etiological factor in the development of carcinoma of the uterus then this atrophic condition ought never to occur in these cases. A study of the records of 116 cases of adeno-carcinoma of the uterus revealed that

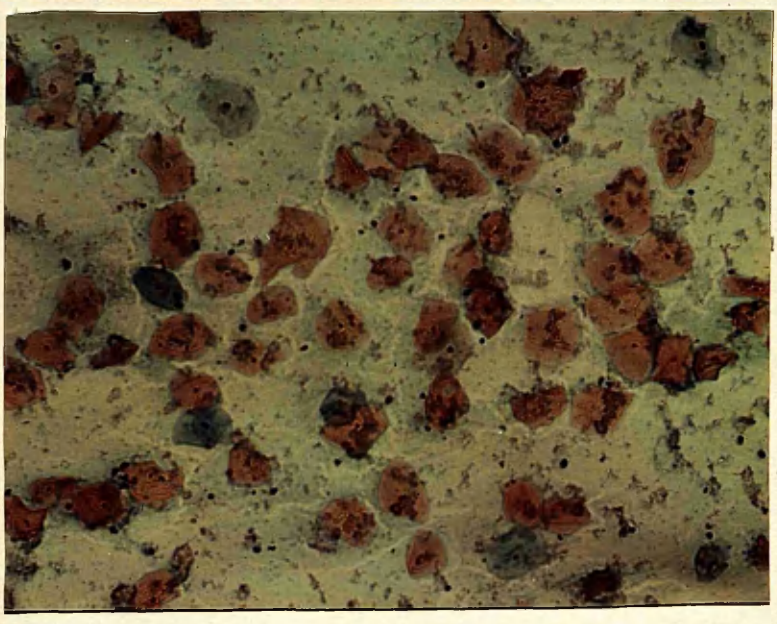
Figure 18.



Vaginal smear from patient with endometrial carcinoma.

Basophilic squamous cells predominate.

Figure 19.



Vaginal smear from patient who had been receiving oestrogen.

Eosinophil squamous cells predominate.

atrophic vaginitis was noted in 18 patients. This is probably a low estimate of the true incidence of atrophic vaginitis in these cases since only those cases which were of gross degree would be noted in the records of patients suffering from a condition of eminently greater importance to the individual's health and life.

There is an important clinical bearing to this association of an atrophic vaginitis with carcinoma of the endometrium which is well illustrated by the following three cases. The first patient when 22 years past the menopause was curetted because of post-menopausal bleeding and a senile endometrial polyp with inactive dilated glands was removed. Twelve years later she complained of further bleeding and a diagnostic curettage was indicated. The vagina and the vaginal aspect of the cervix showed atrophic vaginitis with many minute punctate haemorrhages. When the uterine sound was passed through the cervical canal the fundus of the uterus was perforated and the curettage was abandoned. It was considered that the vaginitis was sufficient to account for the bleeding of which she complained

and the patient was dismissed from hospital. I saw this patient personally three months later and admitted her to hospital immediately. Although the vaginitis was still present curettage was performed. Bulky curettings were obtained and histological examination revealed an adenocarcinoma.

In a further case the correct diagnosis of endometrial carcinoma was delayed because the intense vaginitis complicated by vaginal adhesions was regarded as the source of the bleeding. Curettage was not persisted in when there was difficulty in locating the cervix because of the adhesions.

The third case was that of a diabetic patient who complained of post-menopausal bleeding. A senile vaginitis was present and I had great difficulty in locating the canal in a small atrophic cervix. I was proposing to desist, considering that I had already found an adequate explanation for the bleeding. When however I located the cervical canal and carried out a curettage, bulky friable curettings were obtained from the body of the uterus and a diagnosis of carcinoma was established.

It is especially interesting to note that in

a further case a patient had been curetted 6 years previously when post-menopausal endometrial hyperplasia was found. At the time of the second curettage an endometrial polyp showing an inactive cystic gland pattern with a small associated area of carcinoma was obtained. On this occasion a senile vaginitis was present.

Discussion.

Randall (1945) was impressed by the frequency with which elderly women with endometrial cancer showed a surprisingly well preserved vaginal membrane. He considered that adeno-carcinoma did not develop in the women having hot flushes, with atrophic changes in the vulval and vaginal tissues and with no evidence of oestrogen effect on the endometrium, uterus and vaginal walls. Corscaden (1951) agreed with this view and stated more specifically that he had not found adenocarcinoma of the uterus in a women who at the same time showed an atrophic or senile vaginitis. According to these writers the vagina in patients with endometrial carcinoma has a more youthful appearance than one would expect in women well past the menopause. There is apparently less atrophy,

less pallor and thinning of the vaginal lining. I have several times noticed such a youthful appearance of the vagina and cervix in post-menopausal patients and indeed have for some time made notes in the operation records of these facts. In not one case was endometrial carcinoma present. There are 5 outstanding examples of this finding. Twice the condition was present in the patients who were receiving oestrogen therapy. In the first example the oestrogen was given orally in the form of stilboestrol for a period of over two years. The vaginal smear showed hyper-cornification of the squameous cells and there was endometrial hyperplasia. In the other case the oestrogen had been applied locally in the form of "menopax" ointment for the treatment of pruritis. In one other case the patient had a granulosa cell tumour of the ovary. In the other two cases not only were the vaginal walls healthy but there was abundant secretion of mucus from the cervix. Both patients had an associated hyperplasia of the endometrium. One patient was aged 75 years and both hyperplasia of the endometrium and cervical secretion were noted in an interval of 5 years.

I have found that an atrophic vaginitis is present in an appreciable number of cases of endometrial carcinoma. From a clinical point of view this association is important. Bleeding is usually a symptom of senile vaginitis and while it usually takes the form of a blood stained discharge, the amount of bleeding may on occasion be quite considerable. The assumption that the finding of an atrophic vaginitis rules out the possibility of endometrial carcinoma is unwarranted and dangerous. Even in the presence of an atrophic vaginitis, exploration of the uterus is imperative. If this fact is not appreciated errors in diagnosis will occur and treatment of carcinoma will be delayed. The further importance of this finding is the support it gives for the view that oestrogenic activity, as evidenced by the nutrition of the vagina, is not a prominent feature in endometrial carcinoma.

Summary

1. An investigation of 116 cases of carcinoma of the endometrium was made to discover if there was any close relationship between the condition and hyperplasia of the post-menopausal

endometrium.

2. Study of the previous history of these patients revealed that less than two per cent. had previously suffered from post-menopausal hyperplasia of the endometrium.

3. In 8.4 per cent. of cases studied the uninvolved portion of the endometrium showed hyperplasia. An inactive endometrium accounted for 91.1 per cent. of the total.

4. The literature relating to the association between endometrial polypi and carcinoma was reviewed. As the term "polyp" is a clinical rather than a histological one, this question was dealt with in a consideration of the histological characters of the endometrium and of the polyp.

5. Among the cases in which the endometrium was noted to be inactive, a senile polyp was present in ten instances or 17.9 per cent. of the total.

6. Cases of post-menopausal bleeding were observed over a period of six to twelve years. The incidence of the development of carcinoma subsequent to hyperplasia of the endometrium was

4.1 per cent.

7. The literature referring to the occurrence of endometrial carcinoma in post-menopausal patients having had oestrogen therapy was discussed.

8. Indirect evidence of oestrogen activity, namely the state of nutrition of the vagina, was sought in these cases of carcinoma. In 15.5 per cent. of all cases the vagina was found to be atrophic.

9. No convincing evidence was found to support the view that endometrial carcinoma develops in patients who have had post-menopausal hyperplasia of the endometrium to a greater extent than in patients whose endometrium shows an inactive pattern.

SUMMARY AND CONCLUSIONS.

An investigation of the endometrial patterns found in normal post-menopausal women was considered a necessary preliminary to a consideration of the problem of functional post-menopausal bleeding. It was found that contrary to general opinion simple atrophy of the endometrium was by no means an invariable finding. An inactive state of the endometrium, however, did occur in 98 per cent. of cases. Those cases which were histologically inactive could be divided into two main groups, namely those of simple atrophy which accounted for approximately two thirds of the total, and the remainder in which cystic dilatation of the glands was a prominent feature. In rather less than half of the cases showing an inactive gland pattern the condition was localised to a simple portion of the cavity of the uterus in the form of an endometrial polyp. None of these patterns had any relationship to the age after the menopause when they were discovered. Complete atrophy of the endometrium had occurred in patients one year after the menopause and the cystic gland pattern occurred from one to 34 years after the

cessation of menstruation.

Active hyperplasia of the endometrium was found in less than two per cent. of normal post-menopausal women and when it was present the discovery was made in the early years after the menopause. This may indicate that active hyperplasia in these cases represents a persistence of menopausal hyperplasia associated with terminal anovulatory cycles. It was not possible, however, to obtain a history of excessive or irregular menstruation prior to the menopause in patients whose endometrium later showed hyperplasia.

In view of the diversity of views on the significance of the senile endometrial polyp of a cystic gland pattern evidence was sought relating to the mode of development of such polyps. The dilated gland pattern has frequently been mistaken for hyperplasia although the histological appearance is one of inactivity. There was no statistical evidence to suggest that there was any relationship between active hyperplasia and senile polyps. It would seem that these polyps are merely a localised form of the diffuse cystic gland pattern which is itself a variety of atrophy

of the endometrium. It is significant that a senile endometrial polyp is a normal finding in the endometrium of one post-menopausal women in ten where bleeding has not occurred.

The serious view adopted by gynaecologists of the significance of post-menopausal bleeding is supported by the finding of malignant disease of the uterus and cervix in more than a quarter of cases. Where a benign condition was responsible for the bleeding there was a local extra-uterine source such as decubitus ulceration or polypus of the cervix in many cases. Analysis of the endometrial pattern showed approximately the same incidence of variation as was found in normal post-menopausal women. And in particular the incidence of active hyperplasia was not significantly increased. This indicates that the bleeding originated from the obvious gynaecological lesion and could not be attributed to an altered state of the endometrium.

In some cases of fibroids of the uterus a possible explanation of the bleeding in the post-menopausal patient was found in the position of the fibroid. In the absence of co-existing

endometrial carcinoma or of malignant degeneration in the fibroid itself, a submucous situation of the fibroid was considered to be a factor. This was particularly so when the fibroid had become polypoidal. Where, however, the fibroids were intra-mural it seemed that bleeding was likely to be related to an altered uterine function and the increased incidence of hyperplasia was considered to be of considerable significance.

The group of cases of post-menopausal bleeding referred to as "functional" accounted for approximately 25 per cent. of the total. The striking feature of this group was the high incidence of endometrial hyperplasia which was more than ten times as frequent as in normal post-menopausal women. An important point in this connection was that hyperplasia in patients with bleeding, in contrast to that found in normal women, was not restricted to the early post-menopausal years. On the contrary active hyperplasia in those patients was found as late as 30 years after the cessation of menstruation. It would seem that hyperplasia associated with bleeding is not the persistence of a menopausal condition

but frequently arises de novo in elderly women. In the majority of such cases curettage results in cessation of the bleeding. This may be supplemented by deep X-rays to the ovary. Where haemorrhage recurs after such treatment the most likely cause is the presence of a hitherto unsuspected granulose cell tumour of the ovary, often so small as to be impalpable.

Although hyperplasia was of frequent occurrence in post-menopausal patients with bleeding, this symptom was also present in women whose endometrium showed atrophy or an inactive cystic gland pattern. There was, however , no increase in the incidence of the inactive gland pattern, either of the diffuse type or where the pattern was confined to a polyp, compared with the incidence in normal post-menopausal women. It did not seem that this pattern was responsible for the occurrence of bleeding and it is likely that the discovery in most cases was accidental. The histological structure of the polyps, however, indicated that haemorrhage might result from very slight trauma.

The dilated gland pattern has frequently

been mistaken for hyperplasia although as has been shown, there is no relationship between the two conditions. This has resulted in their incrimination as a cause of post-menopausal bleeding. As a result of erroneous diagnosis of hyperplasia or because of the supposed relationship between the two conditions some of the patients concerned have been subjected to hysterectomy. In fact curettage in addition to supplying the diagnosis constitutes effective treatment. The administration of deep X-rays to the ovaries is neither logical or necessary.

RELATIONSHIP OF HYPERPLASIA TO ENDOMETRIAL CARCINOMA

It was found that there was no evidence that endometrial carcinoma is closely related to the occurrence of post-menopausal hyperplasia of the endometrium. This is contrary to general opinion and the reasons for accepting this view may be stated as follows. Most of the cases reported in the literature in which endometrial carcinoma was noted to follow hyperplasia occurred during the reproductive life. In the cases occurring after the menopause most authors have assumed that in elderly women the endometrium undergoes simple atrophic change. Herein lies the importance of the study of endometriums of normal post-menopausal women. This investigation, as has been stated, showed that cystic dilated glands frequently occur in the normal post-menopausal endometrium. Many writers have not taken this fact into consideration and others have regarded the presence of dilated glands as evidence of hyperplasia, either active or retrogressive. This is especially true of senile polyps which have an inactive appearance and are properly to be classified with atrophic endometrium.

Thus it would appear that many writers have been impressed by the frequent association of an endometrium showing dilated glands with endometrial carcinoma. This they interpreted as being evidence of co-existing hyperplasia and carcinoma, or hyperplasia preceeding the development of malignancy. From this it was argued that the two conditions arose as a result of a common stimulus and that endometrial hyperplasia was a precursor of carcinoma of the corpus uteri. The frequent finding of a cystic gland pattern is confirmed in the present investigation but such an association is only logical when it is remembered that this variety of atrophy of the endometrium occurs under normal conditions in one third of post-menopausal women. This argument applies with equal force to the association between senile endometrial polypi of similar gland pattern with endometrial carcinoma.

The view that there was no close relationship between the two conditions of the endometrium, hyperplasia and carcinoma, received support from a study of cases of hyperplasia over a period of years. It was found that the occurrence of malignancy in an endometrium known to have been

hyperplastic was so infrequent as to suggest that it was a fortuitous circumstance likely to be noted in a consideration of any two commonly occurring abnormalities.

The importance of this interpretation is twofold. To the clinician dealing with a post-menopausal patient with bleeding where the endometrium shows active hyperplasia the problem is simple. If endometrial carcinoma is liable to follow active hyperplasia in an appreciable number of cases then nothing short of complete extirpation of the uterus will constitute adequate treatment. If, however, there is little likelihood of such an occurrence, then the correct treatment is that which will produce cessation of the bleeding. In many cases curettage alone results in cure of the symptoms. Some gynaecologists because of the known action of oestrogens in producing hyperplasia supplement this with X-ray treatment to the ovaries on the assumption that these organs are the source of the hormone. There can be no comparison between the severity of the effects of curettage and of total abdominal hysterectomy in patients of this age group. These elderly women are more likely to

have high blood pressure, impaired kidney function and diminished cardiac reserve. They are more liable to pulmonary congestion and thrombophlebitis with embolism. And in spite of the advances of modern anaesthesia with general supportive measures total hysterectomy is in such patients a formidable operation. In the presence of a malignant condition of the uterus the added risks are accepted, but in the absence of endometrial carcinoma or the probability of its development such radical treatment is unnecessary.

The second consideration is the role of oestrogens in the production of endometrial carcinoma. Oestrogens are known to produce hyperplasia of the endometrium and if this condition were a precursor of carcinoma then the possibility of oestrogens being concerned in the aetiology of the malignant condition would arise. This again is a matter of vital interest to the clinician. Oestrogens are used in the treatment of atrophic conditions of the vagina and vulva of post-menopausal women. The hazard of bleeding from the endometrium during the course of the treatment

must be accepted and the patient should be warned of such a possibility. But, every clinician would hesitate to use a substance which might produce a malignant condition of the endometrium. In spite of the vast amount of oestrogens which have been administered only a very few cases of endometrial carcinoma in such circumstances have been reported, and the relationship of cause and effect was not established.

Finally the occurrence of endometrial carcinoma in post-menopausal patients suffering from atrophic vaginitis is reported. From an aetiological point of view this suggests that there is not in these patients an excess of oestrogen acting on the genital tract. The association of these two conditions receives scanty attention in the literature of the subject. The contrary view, that endometrial carcinoma does not occur in women whose vagina suggests oestrogen deficiency, has been stressed. The clinical implications of this are obvious. The presence of an atrophic vaginitis, while providing a possible explanation of post-menopausal bleeding, should not be accepted as indicating that a malignant process

process of the uterus is unlikely to be present. The necessity for a thorough exploration of the uterine cavity is in no way diminished in these cases.

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Abstracts of Case Histories of patients with fibroids of the uterus in cases of benign postmenopausal bleeding.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. M. McK.	53	47	4	Normal	Atrophic.
Mrs. M.T	55	50	2	"	Atrophic.
Miss J. McL.	54	50	-	"	Atrophic.
Mrs. J.T.	56	49	3	"	Atrophic.
Mrs. J.H.	51	49	4	"	Atrophic.
Miss M.H.	62	49	-	"	Active hyperplasia.
Mrs. J.D.	54	50	-	"	Atrophic.
Miss H.B.	64	50	-	"	Inactive dilated gland.
Mrs. E.C.	60	52	-	"	Inactive dilated gland.
Mrs. G.H.	65	52	2	"	Atrophic.
Mrs. R.W.	45	40	4	X-ray	Secretory endometrium.
Miss G.	69	47	-	Normal	Atrophic.
Miss H. McC.	58	51	-	"	Proliferative endometrium.
Mrs. S. O'H.	53	51	1	"	Atrophic.
Miss H.A.	64	49	-	"	Atrophic.
Mrs. M.R.	60	48	1	"	Atrophic.
Mrs. G.H.	58	54	-	"	Inactive dilated gland.
Mrs. M.G.	51	46	1	"	Proliferative.
Miss C.B.	56	47	-	"	Active hyperplasia.
Mrs. J.B.	50	49	1	"	Secretory endometrium.
Mrs. H.R.	58	47	5	"	Atrophic - fibroid polyp.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Miss S.	47	44	-	Normal	Atrophic.
Miss H.C.	55	51	-	"	Inactive dilated gland.
Mrs. C.McF.	66	43	6	"	Atrophic.
Mrs. J.A.	50	41	2	"	Atrophic - fibroid polyp.
Mrs. W.N.	52	51	1	X-ray	Atrophic.
Mrs. S.G.	49	48	-	Normal	Inactive dilated gland.
Mrs. B.D.	55	51	1	"	Active hyperplasia.
Mrs. J.M.	42	41	-	"	Proliferative.
Mrs. A.B.	50	49	2	"	Atrophic.
Mrs. H.B.	59	56	1	"	Atrophic.
Mrs. G.P.	50	49	1	"	Proliferative endometrium.
Mrs. F.A.	62	50	1	"	Atrophic - fibroid polyp.
Mrs. D.F.	54	52	-	"	Atrophic.
Mrs. S.D.	54	52	2	"	Atrophic.
Mrs. R.M.	67	42	1	"	Inactive dilated gland.
Mrs. A.L.	49	46	2	"	Atrophic.
Mrs. R. McL.	54	50	-	"	Atrophic.
Mrs. S.R.	56	52	-	"	Atrophic.

Abstract of case histories of Functional Postmenopausal Bleeding.

Case	Age	Age at Menopause.	Parity	Type of Menopause.	Histological Findings.
Mrs. McC.	64	55	8	Natural	No endometrium obtained.
Mrs. P.	51	42	3	"	Fibro adenomatous polyp.
Mrs. P.	56	47	2	"	Active hyperplasia.
Mrs. D.	55	51	5	"	Infected active hyperplasia
Mrs. R.	43	41	4	"	Secretory endometrium.
Mrs. G.	59	36	2	"	No endometrium obtained.
Mrs. M.	52	50	1	"	No endometrium obtained.
Mrs. S.	57	50	2	"	No endometrium obtained.
Miss N.	58	51	-	"	No endometrium obtained.
Mrs. S.	62	44	6	"	No endometrium obtained.
Mrs. H.	57	50	1	"	No endometrium obtained.
Mrs. McC.	61	45	3	"	Active hyperplasia.
Mrs. L.	48	45	5	"	No endometrium obtained.
Mrs. H.	46	29	4	Surgical	No endometrium obtained.
Mrs. S.	43	32	4	Surgical	No endometrium obtained.
Mrs. R.	60	51	1	X-ray	Active hyperplasia.
Recurrence of bleeding 3 years later					Active hyperplasia.
Mrs. W.	68	53	7	Natural	No endometrium obtained.
Mrs. S.	59	46	5	"	No endometrium obtained.
Mrs. A.	51	48	13	"	Active hyperplasia.
Mrs. McI.	50	35	4	"	No endometrium obtained.
Mrs. H.	59	40	5	"	Inactive dilated gland.
Mrs. A.	58	45	8	"	No endometrium obtained.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. D.	48	42	2	Natural	Active hyperplasia.
Mrs. F.	61	46	5	X-ray	Active hyperplasia.
Mrs. K.	61	51	6	Natural	Active hyperplasia.
Mrs. M.	55	47	5	"	No endometrium obtained.
Mrs. G.	65	45	8	"	Inactive dilated gland.
Mrs. L.	61	50	2	"	Atrophic endometrium.
Mrs. P.	55	48	2	"	Atrophic endometrium.
Mrs. G.	64	50	9	"	Inactive dilated gland.
Mrs. F.	62	45	1	"	Inactive dilated gland.
Mrs. J.	62	50	4	"	Inactive dilated gland.
Mrs. D.	52	49	4	X-ray	Active hyperplasia.
Curettage at time of menopause - scanty curettings.					
Mrs. W.	58	50	4	Natural	Atrophy.
Mrs. B.	61	50	2	"	No endometrium obtained.
Miss M.	54	49	-	"	No endometrium obtained.
Mrs. F.	57	50	1	"	No endometrium obtained.
Mrs. M.	57	50	5	"	No endometrium obtained.
Mrs. D.	42	40	3	X-ray	No endometrium obtained.
Mrs. W.	60	45	8	Natural	Atrophy.
Mrs. S.	57	45	6	"	No endometrium obtained.
Mrs. B.	51	49	12	"	Active hyperplasia.
Mrs. G.	69	55	5	"	No endometrium obtained.
Mrs. B.	52	43	4	"	No endometrium obtained.
Mrs. B.	69	47	7	"	Inactive dilated gland.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. I.	50	48	2	Natural	Active hyperplasia.
Mrs. S.	50	47	1	"	No endometrium obtained.
Mrs. T.	53	50	4	"	No endometrium obtained.
Mrs. G.	54	50	3	"	Active hyperplasia.
Previous curettage - metropathia haemorrhagica.					
Mrs. B.	60	45	7	Natural	No endometrium obtained.
Mrs. E.	61	38	-	"	Inactive gland pattern.
Mrs. A.	58	40	-	"	Active hyperplasia.
Mrs. L.	50	47	4	"	No endometrium obtained.
Mrs. McF.	66	46	1	"	No endometrium obtained.
Miss S.	53	49	-	Radium	Inactive gland pattern.
Mrs. G.	52	49	3	Natural	Active hyperplasia.
Mrs. S.	48	40	4	"	No endometrium obtained.
Mrs. H.	44	41	3	"	Atrophic endometrium.
Mrs. MacD.	62	52	3	"	Inactive gland pattern.
Mrs. Y.	57	45	4	"	No endometrium obtained.
Mrs. M.	47	45	1	"	Proliferative.
Mrs. S.	55	52	-	"	Fibro adenomatous polyp.
Mrs. D.	51	47	3	"	Active hyperplasia.
Mrs. I.	69	45	2	"	No endometrium obtained.
Mrs. M.	62	50	1	"	Active hyperplasia.
Mrs. I.M.	60	47	9	"	No endometrium obtained.
Mrs. B.R.	67	43	8	"	No endometrium obtained.
Mrs. E.H.	57	50	5	"	No endometrium obtained.
Mrs. S.H.	54	51	2	"	Atrophic endometrium.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. A.F.	62	49	3	Natural	No endometrium obtained.
Mrs. C.W.	58	48	3	"	Active hyperplasia.
Mrs. M.W.	52	51	7	"	No endometrium obtained.
Mrs. J.L.	59	50	4	"	No endometrium obtained.
Mrs. J.L.	50	43	4	"	No endometrium obtained.
Mrs. E.A.	46	43	2	"	No endometrium obtained.
Mrs. M.H.	48	38	6	"	No endometrium obtained.
Mrs. I.D.	56	50	3	"	Infected atrophic endometrium.
Mrs. M.W.	64	42	2	"	Active hyperplasia.
Miss I.T.	64	40	-	"	No endometrium obtained.
Mrs. C.G.	44	40	8	Surgical	Atrophic endometrium.
Mrs. A.K.	52	51	10	Natural	No endometrium obtained.
Mrs. S.D.	54	40	11	"	No endometrium obtained.
Mrs. A.A.	70	46	5	"	Infected inactive cystic gland
Mrs. J.F.	49	29	2	Surgical	No endometrium obtained.
Mrs. C.A.	67	42	2	Natural	Atrophic endometrium.
Mrs. M.S.	57	45	6	"	No endometrium obtained.
Mrs. E.G.	52	51	2	"	Atrophic endometrium.
Mrs.M.McT.	54	52	3	"	No endometrium obtained.
Mrs. A.D.	52	48	3	"	No endometrium obtained.
Mrs. N.M.	50	46	9	"	No endometrium obtained.
Miss M.C.	77	46	-	"	No endometrium obtained.
Mrs. C.F.	57	38	-	"	No endometrium obtained.
Mrs.M.McG.	61	55	2	"	Active hyperplasia.
Recurrence of bleeding 2 years later					No endometrium.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. F. McC.	60	45	4	Natural	Active hyperplasia.
	Recurrence of bleeding 6 months later				No endometrium.
Mrs. A.V.	52	46	3	Natural	Secretory.
Mrs. A.G.	70	50	3	"	Atrophic endometrium.
Mrs. C.	61	48	4	"	Active hyperplasia.
Mrs. A.L.	53	44	-	Surgical	Inactive dilated gland.
Miss S.K.	67	41	-	Natural	Active hyperplasia.
Mrs. J.I.	46	34	1	"	No endometrium.
Mrs. M.S.	54	52	9	"	No endometrium.
Mrs. M.M.	58	52	2	"	Atrophic endometrium.
Mrs. J.P.	70	50	4	"	Infected active hyperplasi
	(4 years later admitted because of twisted ovarian cyst - found to be a granulosa cell tumour).				
Mrs. E.M.	63	43	6	Natural	Atrophic endometrium.
Mrs. M. McI.	72	50	3	"	Atrophic endometrium.
Mrs. J.K.	51	40	-	"	Atrophic endometrium.
Mrs. M.W.	56	39	4	"	Atrophic endometrium.
Mrs. M. McI.	56	46	6	"	Active hyperplasia.
Mrs. M.B.	55	54	5	"	Atrophic endometrium.
Mrs. E. McI.	47	46	1	"	Secretory endometrium.
Miss E.C.	52	49	-	"	Inactive dilated gland.
Mrs. C.R.	48	46	4	"	Proliferative endometrium
Mrs. C.A.	60	40	-	"	No endometrium.
Mrs. J.J.	60	48	5 + 1	"	Infected atrophic endometrium.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. M.C.	50	45	-	Natural	Active hyperplasia.
Mrs. M.R.	58	48	5	"	No endometrium.
Miss I.S.	69	40	-	"	No endometrium.
Mrs. E.B.	61	54	2	X-ray	Atrophic endometrium.
Mrs. A. McC.	50	46	4	Natural	Active hyperplasia.
(Treated by Radium. 5 years later curettage before repair - no endometrium).					
Mrs. M.L.	55	49	9	Natural	No endometrium.
Mrs. P.F.	60	50	3	"	No endometrium.
Mrs. C.	58	48	-	"	Infected inactive dilated gland.
Mrs. T.	52	48	1	"	Proliferative endometrium - infected.
Mrs. A.H.	53	47	-	"	No endometrium.
Mrs. E.C.	69	47	10	"	Inactive cystic gland.
(Two years later recurrence of bleeding. Active hyperplasia).					
Mrs. E. McD.	50	45	3	Radium	No endometrium.
Mrs. M. McC.	74	47	-	Natural	Active hyperplasia.
Mrs. B.	47	45	-	"	No endometrium.
Mrs. M.K.	55	52	1	"	Inactive dilated glands.
Mrs. E. McC.	58	48	3	"	No endometrium.
Mrs. H.O.	61	42	6	"	Atrophic endometrium.
Mrs. S.L.	62	1	50	"	Atrophic endometrium.
Mrs. I.B.	66	46	9	"	No endometrium.
Mrs. A.B.	53	46	1	"	No endometrium.
Mrs. B.L.	48	37	1	"	No endometrium.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. D.S.	70	50	6	Natural	Inactive gland pattern.
Mrs. J.C.	49	45	6	"	Infected inactive gland pattern.
Mrs. J.H.	43	40	2	"	Active hyperplasia.
Mrs. St. I.	54	50	2	"	No endometrium.
Mrs. B.W.	61	34	1	"	No endometrium.
Mrs. H. McL.	79	50	4	"	No endometrium.
Mrs. S.H.	53	46	1	X-ray	No endometrium.
Mrs. J.M.	54	50	5	Natural	Active hyperplasia.
Mrs. S.S.	58	48	-	"	Active hyperplasia.
(3 yrs. later had recurrence of bleeding - adenocarcinoma).					
Mrs. J.C.	65	50	11	Natural	Active hyperplasia.
Mrs. P.D.	60	50	9	"	No endometrium.
Mrs. G.D.	59	49	7	"	No endometrium.
Mrs. M.W.	54	51	-	"	Atrophic endometrium.
Mrs. E.W.	62	48	2	"	Active hyperplasia.
(7 years later recurrence of bleeding - endometrial carcinoma).					
Mrs. H.T.	63	52	5	Natural	Active hyperplasia.
Mrs. H.W.	51	46	1	"	Active hyperplasia.
Mrs. E.W.	69	40	6	"	No endometrium.
Mrs. E.S.	57	50	9	"	No endometrium.
Mrs. C.F.	59	50	2	"	No endometrium.
Mrs. R.W.	59	47	-	"	Inactive dilated gland.
Mrs. S.L.	65	47	2	"	No endometrium.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. C. McD.	52	50	4	Natural	No endometrium.
Mrs. E.W.	73	50	1	"	Active hyperplasia.
Mrs. R.W.	59	50	1	"	Active hyperplasia.
Mrs. D.A.	52	51	7	"	Proliferative endometrium.
Mrs. E.B.	63	45	3	"	Fibro adenomatous polyp.
Mrs. A.T.	58	50	-	"	No endometrium.
Mrs. H. McC.	59	47	4	"	No endometrium.
Mrs. C.A.	71	50	9	"	Inactive dilated glands.
Mrs. A.C.	54	46	2	"	Active hyperplasia.
Mrs. J.B.	62	42	-	"	Fibro adenomatous polyp.
Mrs. C.L.	51	49	1	"	Atrophic endometrium.
Mrs. R.T.	57	30	2	"	No endometrium.
Mrs. A.S.	57	50	3	"	No endometrium.
Mrs. I. McN.	51	49	2	"	Infected atrophic endometriu
Mrs. L.A.	47	43	2	"	Atrophic endometrium.
Mrs. J.G.	51	40	3	"	No endometrium.
Mrs. C.McD.	67	47	6	"	Active hyperplasia.
Mrs. A.S.	54	46	1	"	No endometrium.
Mrs. B.F.	45	42	6	"	Active hyperplasia.
Mrs. S.D.	52	48	-	"	No endometrium.
Miss A.A.	54	49	-	"	Fibro adenomatous polyp.
Mrs. A. McM.	61	50	4	"	Inactive dilated gland.
Mrs. S.B.	58	48	1	"	Active hyperplasia.
Mrs. C.B.	50	48	2	"	Active hyperplasia.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. A.W.	61	47	2	Natural	Active hyperplasia.
Mrs. W.P.	73	48	2	"	Inactive dilated gland.
Mrs. H.K.	51	47	8	"	Active hyperplasia.
Mrs. C.H.	63	50	3	"	No endometrium.
Mrs. I. McF.	68	52	6	"	No endometrium.
Mrs. I.B.	73	50	6	"	No endometrium.
Miss J.B.	55	50	-	"	No endometrium.
Mrs. H.M.	58	36	5	"	No endometrium.
Mrs. C.F.	42	36	2	Surgical	Active hyperplasia.
Miss J. McA.	52	50	-	Natural	No endometrium.
Mrs. A.B.	51	46	4	"	No endometrium.
Mrs. A.F.	75	50	4	"	Active hyperplasia.
Recurrence 5 years later					Active hyperplasia.
Mrs. G.M.	53	47	6	Natural	Active hyperplasia.
Mrs. C.H.	69	53	3	"	No endometrium.
Mrs. S. McW.	46	40	1	"	No endometrium.
Mrs. L.L.	53	50	4	"	No endometrium.
Mrs. I. McC.	64	51	2	"	Fibro adenomatous polyp.
Mrs. H.W.	47	45	2	"	Active hyperplasia.
Mrs. A.W.	52	45	5	"	Atrophic endometrium.
Mrs. K.D.	49	46	-	"	No endometrium.
Mrs. J.M.	50	48	3	Radium	Proliferative endometrium.
Miss S.S.	60	48	-	Natural	No endometrium.
Mrs. A.M.	52	50	4	X-ray	Atrophic endometrium.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. A.C.	59	47	3	Natural	Active hyperplasia.
Mrs. C.W.	80	62	-	"	Inactive gland pattern.
Mrs. A. McB.	60	44	1	"	Active hyperplasia.
Mrs. I. McG.	54	52	4	"	No endometrium.
Mrs. B.A.	54	49	7	"	No endometrium.
Mrs. J.M.	50	45	3	"	Atrophic.
Mrs. I.H.	50	49	5	"	Infected atrophic.
Mrs. H.S.	49	45	2	"	Atrophic.
Mrs. S.B.	53	51	-	X-ray	Inactive dilated gland.
Mrs. A.W.	51	48	1	Natural	No endometrium.
Mrs. H.B.	50	45	3	"	Active hyperplasia.
Mrs. H. McC.	63	48	4	"	No endometrium.
Mrs. I.W.	59	50	-	"	No endometrium.
Mrs. R.A.	53	44	2	"	No endometrium.
Mrs. A. McG.	52	49	7	"	Atrophic.
Mrs. H.K.	68	50	3	"	Atrophic.
Mrs. R.W.	44	41	2	"	Proliferative.
Mrs. C.A.	72	50	5	"	Inactive dilated gland.
Mrs. K.B.	54	46	-	"	No endometrium.
Miss A.B.	52	50	-	"	Inactive dilated gland.
Mrs. M.T.	48	41	3	"	Active hyperplasia.
Mrs. J.B.	48	47	1	"	No endometrium.
Mrs. A.W.	51	49	4	"	Active hyperplasia.
Mrs. C.A.	55	41	2	"	Active hyperplasia.
Mrs. A.S.	49	47	7	"	No endometrium.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. A.F.	55	51	3	Natural	Active hyperplasia.
Mrs. K.B.	66	50	1	"	Inactive dilated gland.
Mrs. R.A.	43	42	3	"	Active hyperplasia.
Mrs. C.T.	54	52	9	"	No endometrium.
Mrs. H. McC.	60	50	2	"	Proliferative endometrium.
Mrs. W.S.	56	44		X-ray	Active hyperplasia.
		Previous metropathia haemorrhagica 11 years ago.			
Mrs. S. McA.	50	52	6	Natural	No endometrium.
Mrs. H.F.	63	45	-	"	No endometrium.
Mrs. C. McD.	54	50	2	"	Active hyperplasia.
Mrs. A.M.	65	45	4	"	No endometrium.
Mrs. H.T.	69	54	-	"	No endometrium.
Mrs. K. McM.	49	47	2	"	No endometrium.
Mrs. R.B.	50	49	8	"	No endometrium.
Mrs. A.Y.	53	44	3	"	Active hyperplasia.
Mrs. H.B.	50	49	11	"	No endometrium.
Mrs. H.R.	52	51	4	"	Atrophy.
Mrs. A.B.	50	45	-	"	No endometrium.
Mrs. A.B.	50	49	5	"	No endometrium.
Mrs. R.H.	55	48	2	"	No endometrium.
Mrs. R.M.	52	51	4	X-ray	Atrophic endometrium.
Mrs. W.H.	53	51	2	Natural	Proliferative.
Mrs. A.M.	62	42	1	"	Active hyperplasia.
Mrs. A.J.	59	40	5	"	Active hyperplasia.
Mrs. H.M.	65	50	2	"	Atrophic endometrium.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. H.C.	70	59	1	Natural	Infected atrophic endometrium.
Mrs. R.R.	57	52	-	"	Atrophic endometrium.
Mrs. B. McN.	47	44	4	"	Infected hyperplasia.
Mrs. G.F.	54	52	2	"	Active hyperplasia.
Mrs. B.T.	54	50	-	"	No endometrium.
Mrs. G.C.	51	48	7	"	No endometrium.
Mrs. H.T.	54	48	1	X-ray	Inactive dilated gland.
Mrs. T.G.	50	49	4	Natural	Atrophic endometrium.
Mrs. S.W.	52	47	3	"	Secretory endometrium.
Mrs. I. McF.	68	46	1	"	Proliferative endometrium.
Mrs. H. McL.	40	36	4	"	Secretory endometrium.
Mrs. S.B.	51	49	1	"	Secretory endometrium.
Mrs. H. McA.	61	47	7	"	Atrophic endometrium.
Mrs. C. McK.	66	50	3	"	Active hyperplasia.
Miss A.W.	42	38	1	"	Atrophic endometrium.
Mrs. A. McL.	57	47	2	"	Active hyperplasia.
Miss C.Y.	52	51	-	"	Infected inactive dilated gland.
		Hyperplasia in polyp 3 years previously.			
Mrs. M.F.	69	42	3	Natural	Active hyperplasia.
Mrs. H.P.	54	45	4	"	Active hyperplasia.
Mrs. H.G.	57	55	2	"	Atrophic endometrium.
Mrs. M.C.	54	48	-	"	Inactive dilated gland.
		(Metropathia haemorrhagica 4 years previously).			
Mrs. H.R.	60	48	7	Natural	No endometrium.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. M.R.	57	45	2	Natural	No endometrium.
Mrs. A.C.	55	52	1	"	Inactive dilated gland.
Mrs. H.H.	66	47	-	"	No endometrium.
Mrs. M.M.	58	52	4	"	No endometrium.
Mrs. A. McD.	52	48	7	"	No endometrium.
Mrs. I. McG.	52	48	4	"	Proliferative endometrium.
Mrs. C.G.	54	48	13	"	Atrophic.
Mrs. A. McL.	63	56	-	"	No endometrium.
Mrs. J.B.	53	52	5	"	Atrophic.
Mrs. H.M.	64	43	4	"	No endometrium.
Mrs. M.C.	60	40	2	"	No endometrium.
Mrs. I.B.	52	49	2	"	Active hyperplasia.
Mrs. B.G.	52	50	3	"	Active hyperplasia.
Mrs. M.B.	50	54	3	"	Atrophic.
Mrs. M.H.	60	42	5	"	Inactive dilated gland.
Mrs. I.G.	51	47	1	"	Active hyperplasia.
Mrs. H.L.	47	46	1	"	No endometrium.
Mrs. A.McN.	62	51	5	"	No endometrium.
Mrs. M.H.	53	42	1	"	No endometrium.
Mrs. S.G.	51	45	4	"	Inactive dilated gland.
Miss A.A.	53	51	-	"	Active hyperplasia.
Mrs. H.M.	51	44	5	"	Proliferative.
Mrs. S.C.	74	47	6	"	Inactive dilated gland.
Mrs. A.G.	53	51	5	"	Active hyperplasia.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. M.C.	68	46	-	Natural	Inactive dilated gland.
Mrs. H.C.	55	49	1	"	Inactive dilated gland.
Mrs. B.M.	60	46	5	"	Inactive dilated gland.
Mrs. H. McG.	71	46	1	"	Active hyperplasia.
Mrs. A.S.	46	43	1	X-ray	Atrophic.
Mrs. M.S.	59	52	1	Natural	No endometrium.
Mrs. M.F.	62	50	2	"	Proliferative.
Mrs. I. McM.	49	46	4	"	Proliferative.
Mrs. A.B.	71	52	8	"	Infected inactive dilated gland
Mrs. S.F.	52	46	3	"	Inactive dilated gland.
Mrs. S.M.	58	44	3	"	Atrophic.
Mrs. H.F.	49	48	3	"	Inactive dilated gland.
Mrs. H.A.	54	50	3	"	Active hyperplasia.
Mrs. M.C.	56	54	4	"	Atrophic.
Mrs. W.H.	49	47	5	"	No endometrium.
Mrs. L. McC.	48	44	3	"	Atrophic.
Mrs. W.C.	54	48	-	"	No endometrium.
Mrs. H.L.	61	52	1	"	No endometrium.
Mrs. I.D.	60	50	6	"	Inactive dilated gland.
Mrs. C. McK.	48	47	4	"	No endometrium.
Miss M.E.	66	28	-	"	Atrophic.
Mrs. I.I.	53	50	4	"	Proliferative.
Mrs. H.R.	55	50	2	"	Inactive dilated gland.
Mrs. S. McC.	56	55	6	"	Proliferative.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. A.M.	55	40	-	Natural	Inactive dilated gland.
Mrs. H.M.	52	42	1	"	No endometrium.
Mrs. M.R.	51	45	1	"	Active hyperplasia.
Mrs. G.W.	45	43	4	"	No endometrium.
Mrs. H.B.	51	49	4	"	No endometrium.
Mrs. I.S.	62	49	6	"	Atrophic.
Mrs. M.B.	51	49	5	"	No endometrium.
Mrs. K.A.	49	47	3	"	Proliferative.
Mrs. J.D.	51	47	1	X-ray	Atrophic.
Mrs. K.W.	56	45	-	Natural	Inactive dilated gland.
Mrs. J.B.	54	42	3	Surgical	Atrophic.
Mrs. J.F.	52	48	9	Natural	Atrophic.
Mrs. E.G.	56	42	2	"	Active hyperplasia.
Mrs. K.B.	49	42	1	"	Atrophic.
Mrs. E.R.	47	41	1	"	No endometrium.
Mrs. J.R.	78	50	8	"	Atrophic.
Mrs. A.M.	49	45	1	"	No endometrium.
Mrs. A.F.	51	44	2	"	No endometrium.
Mrs. J. McQ.	60	50	4	"	Fibro adenomatous polyp.
Mrs. C.A.	61	53	1	"	Inactive dilated gland.
Mrs. J.M.	62	48	3	"	No endometrium.
Mrs. K. McG.	60	52	1	"	Atrophic.
Mrs. R.C.	53	52	1	"	Infected inactive dilated gland.
Mrs. E.W.	51	42	2	"	Proliferative.
Mrs. H.N.	52	51	4	"	No endometrium.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. A.W.	62	48	2	Natural	Atrophic.
Mrs. H.B.	54	51	7	"	Atrophic.
Mrs. A.C.	55	44	3	"	Inactive dilated gland.
Mrs. E.C.	60	51	3	"	Active hyperplasia.
Mrs. H.S.	54	50	6	"	No endometrium.
Mrs. H.W.	63	47	1	"	Infected atrophic.
Mrs. I.G.	52	49	2	"	Atrophic.
Mrs. S.B.	49	48	4	"	No endometrium.
Mrs. H.C.	52	47	2	"	No endometrium.
Mrs. H.N.	52	48	3	"	Proliferative.
Mrs. A. McK.	61	50	7	"	No endometrium.
Mrs. H. McS.	49	39	3	Surgical	Atrophic.
Mrs. S.R.	52	48	2	Natural	Proliferative.
Mrs. E.M.	52	50	1	"	Proliferative.
Mrs. S.D.	47	45	4	"	Active hyperplasia.
Mrs. H.F.	55	21	2	Surgical	Atrophic.
Mrs. E. McG.	59	53	2	"	Inactive gland pattern.
Mrs. S.S.	64	45	3	"	Atrophic.
Mrs. H.T.	52	45	1	X-ray	Atrophic.
Mrs. E.L.	72	52	7	Natural	No endometrium.
Mrs. H.Y.	70	50	5	"	Atrophic.
Mrs. H.K.	60	54	3	"	Inactive dilated gland.
Mrs. A.R.	41	40	2	Surgical	Inactive dilated gland.
Mrs. H.W.	62	51	4	Natural	Inactive dilated gland.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. E.W.	59	43	7	Natural	Atrophic.
Mrs. J.B.	50	48	3	"	No endometrium.
Mrs. R.W.	44	43	3	X-ray	Fibro adenomatous polyp.
Mrs. H. McL.	51	48	2	Natural	No endometrium.
Mrs. R.A.	47	45	1	"	No endometrium.
Mrs. R.W.	64	51	-	"	No endometrium.
Mrs. H.M.	57	54	2	"	Active hyperplasia.
Mrs. E.L.	60	48	4	"	No endometrium.
Mrs. K.C.	53	51	2	"	Inactive dilated gland.
Mrs. C.C.	54	52	3	"	Atrophic.
Mrs. H.S.	48	47	2	"	Active hyperplasia.
Mrs. A.W.	65	43	1	"	Infected active hyperplasia.
Mrs. H. McD.	51	50	3	"	Atrophy - tuberculosis.
Mrs. H.B.	49	47	3	"	Active hyperplasia.
Mrs. W.S.	50	49	2	"	Atrophic.
Mrs. A.Y.	51	49	2	"	Atrophic.
Mrs. H.L.	50	49	3	"	Proliferative.
Mrs. R.T.	49	47	1	"	Infected proliferative.
Mrs. M.P.	53	51	6	"	Infected active hyperplasia.
Mrs. E.T.	51	46	4	"	Atrophic.
Mrs. H.F.	50	48	2	"	Active hyperplasia.
Mrs. I.H.	57	47	8	"	No endometrium.
Mrs. A. McC.	58	49	2	"	Infected atrophic.
Mrs. A.M.	54	52	3	"	Atrophic.
Mrs. S.P.	51	42	4	X-ray	Inactive dilated gland.

(9 years previously menorrhagia - D. & C. premenstrual endometrium).

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. E.H.	51	42	1	X-ray	Atrophic.
Mrs. B.G.	63	52	2	Natural	No endometrium.
Mrs. M.G.	47	45	3	"	No endometrium.
Mrs. R.L.	51	46	-	"	No endometrium.
Mrs. A. McC.	53	52	1	"	Atrophic.
Miss A.S.	64	50	7	"	No endometrium.
Mrs. R.M.	52	41	1	"	No endometrium.
Mrs. C.G.	64	49	1	"	No endometrium.
Mrs. A.D.	71	50	3	"	No endometrium.
Mrs. A.K.	54	52	4	"	No endometrium.
Mrs. I.T.	54	48	-	"	No endometrium.
Mrs. E. McC.	48	46	7	"	No endometrium.
Mrs. R. McL.	57	52	3	"	Atrophic.
Mrs. R.D.	68	45	-	"	Proliferative tuberculosis.
Mrs. A. McF.	70	42	8	"	Inactive dilated gland.
Mrs. J.L.	48	42	8	"	No endometrium.
Mrs. E.A.	63	51	3	"	No endometrium.
Mrs. M.F.	52	50	1	"	No endometrium.
Mrs. W.G.	57	47	3	"	Active hyperplasia.
Mrs. L. McB.	54	50	3	"	Inactive dilated gland.
Mrs. H.W.	52	50	1	"	Proliferative.
Mrs. A.G.	52	48	2	"	Active hyperplasia.
Mrs. E.F.	50	44	3	"	Infected inactive dilated gland.
Mrs. K.A.	60	53	2	"	Inactive dilated gland.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. B.C.	60	50	4	Natural	Fibro adenomatous pol
Mrs. W.R.	62	47	1	"	Atrophic tuberculosis
Mrs. P. McC.	64	42	3	"	No endometrium.
Mrs. D.P.	55	51	7	"	No endometrium.
Mrs. R.G.	56	51	1	"	No endometrium.
Mrs. G.M.	52	48	-	"	No endometrium.
Mrs. K.W.	46	45	4	"	Proliferative.
Mrs. E.A.	62	47	1	"	Inactive dilated glan
Mrs. I.W.	57	52	2	"	Active hyperplasia - tuberculosis.
Mrs. E.G.	54	42	4	"	Active hyperplasia.
Mrs. G.F.	55	50	9	"	No endometrium.
Mrs. N.S.	57	47	3	"	Active hyperplasia.
Mrs. G.P.	53	50	4	"	No endometrium.
Mrs. H.S.	64	50	1	"	No endometrium.
Mrs. S.S.	72	39	2	"	Atrophic.
Mrs. S.C.	53	51	4	"	Atrophic.
Mrs. R.M.	56	49	2	"	Active hyperplasia.
Mrs. M.C.	51	50	1	"	Atrophic.
Mrs. M.S.	54	53	3	"	Fibro adenomatous pol
Mrs. E.C.	59	44	2	"	Inactive dilated glan
Mrs. I.W.	54	49	5	"	Atrophic.
Mrs. S.R.	48	45	1	"	No endometrium.
Mrs. H.K.	50	49	2	"	Active hyperplasia.
Mrs. E.McP.	64	49	4	"	Active hyperplasia.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. A.S.	61	51	3	Natural	Inactive dilated gland.
Mrs. S.D.	52	48	2	"	Atrophic.
Mrs. H. McE.	72	48	1	"	No endometrium.
Mrs. L.C.	70	50	3	"	Inactive dilated gland.
Mrs. H.F.	58	38	1	X-ray	Inactive dilated gland.
Mrs. H.N.	61	57	6	Natural	Inactive dilated gland.
Mrs. H. McD.	53	47	2	"	Atrophic.
Mrs. W.S.	72	50	3	"	No endometrium.
Mrs. A. McI.	64	48	1	"	No endometrium.
Mrs. H.R.	69	50	4	"	Atrophic.
Mrs. G. McL.	66	50	2	"	Fibro adenomatous polyp.
Mrs. E.C.	51	47	3	"	Atrophic.
Mrs. M.B.	56	53	1	"	Atrophic.
Mrs. A. McG.	55	36	2	"	Active hyperplasia.
Mrs. E.A.	62	52	4	"	Atrophic.
Mrs. M. McA.	56	49	2	"	Fibro adenomatous polyp.
(Curettage one year previously - no endometrium).					
Mrs. J.H.	54	50	3	Natural	No endometrium.
Mrs. W.A.	62	45	1	"	No endometrium.
Mrs. J.P.	54	51	1	"	Active hyperplasia.
Mrs. A. McG.	53	50	1	"	Infected inactive dilated gland.
Mrs. I.M.	53	51	4	"	Atrophic.
Mrs. G.B.	55	51	2	"	Inactive dilated gland.
Mrs. S.M.	51	47	3	"	Inactive dilated gland.
Mrs. E.H.	52	50	1	"	Atrophic.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. I.D.	52	51	3	Natural	Active hyperplasia.
Mrs. S.T.	51	49	3	"	Inactive dilated gland.
Mrs. G.L.	57	46	2	"	Active hyperplasia.
Mrs. M.A.	46	39	3	"	Atrophic.
Mrs. E.G.	54	52	1	"	Inactive dilated gland.
Miss A. McF.	78	52	1	"	Infected atrophic.
Mrs. J.W.	64	45	3	"	No endometrium.
Mrs. E.L.	70	50	3	"	Inactive dilated gland.
Mrs. G. McL.	67	49	6	"	Inactive dilated gland.
Mrs. A.M.	64	50	5	"	No endometrium.
Mrs. M.T.	48	46	8	"	Atrophic.
Mrs. G.L.	54	43	2	"	No endometrium.
Mrs. B.A.	66	51	6	"	No endometrium.
Mrs. J.L.	65	53	9	"	Active hyperplasia, infected.
Mrs. A.M.	50	49	9	"	Atrophic.
Mrs. J.C.	60	50	3	"	Active hyperplasia.
Mrs. J. McC.	51	49	4	"	Active hyperplasia.
Mrs. S.K.	51	49	9	"	Active hyperplasia.
Mrs. M.B.	58	48	3	"	Atrophic.
Mrs. G.H.	67	49	1	"	Atrophic.
Mrs. E.H.	54	52	6	"	Inactive dilated gland.
Mrs. M.D.	68	44	5	"	Inactive dilated gland.
Mrs. H. McL.	58	40	-	"	No endometrium.
Mrs. E.M.	59	54	2	"	Inactive dilated gland.
Mrs. H.D.	50	45	4	Radium	Atrophic.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Mrs. J.G.	54	52	1	Natural	Inactive dilated gland.
Mrs. J.C.	64	45	9	"	Inactive dilated gland.
Mrs. I.H.	55	52	3	"	Inactive dilated gland.
Mrs. J.C.	48	46	3	"	No endometrium.
Mrs. H.H.	70	50	-	"	No endometrium.
Mrs. G.T.	61	49	4	"	No endometrium.
Mrs. J.G.	51	49	2	"	Fibro adenomatous polyp.
Mrs. S.S.	54	46	4	"	Atrophic tuberculosis.
Mrs. H.O.	60	51	3	"	No endometrium.
Mrs. E.C.	45	42	5	"	No endometrium.
Mrs. J.B.	56	53	3	"	Secretory.
Mrs. W.H.	54	47	3	"	No endometrium.
Mrs. A.G.	46	44	4	"	Active hyperplasia.
Mrs. E.S.	64	42	2	"	Active hyperplasia.
Mrs. H.A.	60	51	3	"	No endometrium.
Mrs. H. McG.	47	41	10	"	Proliferative.
Mrs. G.H.	57	50	2	"	Fibro adenomatous polyp.
Mrs. E.D.	56	51	5	"	Inactive dilated gland.
Mrs. J.M.	50	49	3	"	Active hyperplasia.
Mrs. S.C.	54	47	4	"	Inactive dilated gland.
Mrs. J.C.	71	55	10	"	Atrophic.
Mrs. E.C.	44	40	1	"	Infected fibro adenomatous polyp.
Mrs. C.R.	62	50	8	"	Active hyperplasia.
Mrs. F.B.	45	42	2	"	Active hyperplasia.

Case	Age	Age at Menopause	Parity	Type of Menopause	Histological Findings.
Miss W.R.	49	47	-	Natural	No endometrium.
Mrs. C.H.	62	54	3	"	No endometrium.
Mrs. R.F.	57	50	-	"	No endometrium.
Mrs. H.L.	70	50	1	"	No endometrium.
Mrs. C.C.	50	47	7	"	Active hyperplasia.
Miss V.R.	55	52	1	"	No endometrium.
Mrs. M.G.	60	49	1	"	Inactive dilated gland.
Mrs. H.B.	60	50	3	"	Active hyperplasia.
Mrs. E.C.	74	47	6	"	Inactive dilated gland.
Mrs. S.H.	58	54	3	"	Active hyperplasia.
Mrs. P.G.	51	45	4	"	Inactive dilated gland.
Mrs. H. McN.	62	51	5	"	Atrophy.
Mrs. P.H.	49	46	1	"	No endometrium.
Mrs. E.L.	47	46	1	"	Active hyperplasia.
Mrs. J.H.	60	42	5	"	Active hyperplasia.
Mrs. S.G.	52	50	3	"	Active hyperplasia.
Mrs. N.C.	55	52	4	"	Inactive dilated gland.
Mrs. H.P.	55	49	3	"	Inactive dilated gland.
Mrs. H.R.	42	40	2	X-ray	Secretory.
Mrs. W.J.	58	49	6	Radium	Fibro adenomatous polyp.

Abstracts of Case Histories of patients with postmenopausal bleeding receiving oestrogen.

Case	Age	Age at Menopause	Parity	Menopause	Medication	Duration	Indication	Histological Findings.
Mrs. M.E.	62	42	4	Natural	Stilboestrol	?	?	Inactive dilated gland.
Mrs. J.A.	55	52	2	"	"	18 mths.	"Flushings"	Active hyperplasia.
Mrs. H.T.	45	41	2	"	"	4 yrs.	"	No endometrium obtained.
Mrs. M.M.	58	52	1	"	"	2 mths.	?	Active hyperplasia.
Mrs. H.K.	56	50	2	"	"	?	"Flushings"	Inactive dilated gland.
Mrs. W.I.	54	50	2	"	"	3 mths.	?	No endometrium obtained.
Mrs. M.R.	46	42	-	"	"	?	?	Active hyperplasia.
Mrs. A.R.	52	47	-	"	"	2 mths.	Pruritus	Inactive dilated gland.
Mrs. W.D.	54	45	2	"	"Menopax"	4 mths.	"	No endometrium obtained.
Mrs. A.G.	60	50	-	"	Stilboestrol	5 mths.	?	Atrophy.
Mrs. B.L.	71	51	3	"	"	6 mths.	Arthritis	Active hyperplasia.
Mrs. J.K.	68	50	2	"	"	6 mths.	Kraurosis	No endometrium obtained.
Mrs. B.S.	55	47	1	"	"	5 mgm.b.d. 3 weeks	Pre-op. Medication	No endometrium obtained.
Mrs. S.H.	56	50	4	"	"	?	?	Active hyperplasia.
Mrs. J.I.	74	51	9	"	"	?	"Flushings"	Atrophy.
Mrs. J.B.	57	45	4	"	"	1 year	?	Atrophy.

Case	Age	Age at Menopause	Parity	Menopause	Medication	Duration	Indication.	Histological Findings.
Mrs. M.K.	51	40	-	Natural	Stilboestrol	6 mths.	?	Inactive dilated gland.
Mrs. R.W.	54	50	1	X-ray	"	?	"Flushings"	Atrophy.
Mrs. H.O.	71	50	9	Natural	"	1 year	?	No endometrium obtained.
Mrs. H.J.	60	51	4	"	"	5 mgm.b.d.) 4 weeks)	Pre-op. Medication	Active hyperplasia.
Mrs. J.E.	62	53	-	"	"Menopax"	6 mths.	Pruritus	Inactive dilated gland.
Mrs. S.T.	52	48	1	X-ray	Stilboestrol	5 mgm.b.d.) 3 weeks)	Pre-op. Medication.	Proliferative.
Mrs. M.W.	60	52	3	Natural	"Menopax"	3 mths.	Vulvitis	Atrophy.
Mrs. A.K.	71	55	1	"	Stilboestrol	?	Leukoplakia	No endometrium obtained.
Mrs. E.R.	50	45	4	"	"Menopax"	?	Vulvitis	Active hyperplasia.
Mrs. J.McK.	60	52	-	"	Stilboestrol	?	"	No endometrium obtained.
Mrs. R.M.	52	47	3	"	"	?	?	Active hyperplasia.
Mrs.M.G.	70	63	1	"	"	4 mths.	"Flushings"	Proliferative.
Mrs. A.D.	50	45	2	"	"Menopax"	4 mths.	?	Atrophy.

Abstracts of case histories of patients with endometrial carcinoma.

Name.	Age	Age at Menopause	Condition of vagina	Duration of Bleeding	Uninvolved endometrium.
Miss J. McM.	63	51	Normal	3 weeks	Inactive dilated gland.
Miss G.B.	62	42	"	1 yr. 3 mths.	-
Mrs. J.F.	56	52	"	5 months	Atrophic.
Mrs. E.I.	56	47	"	5 months	Atrophic.
Mrs. H.L.	59	49	"	1 year	-
Mrs. A.S.	54	45	"	2 years	Inactive dilated gland.
Miss P.W.	69	52	"	5 months	Inactive dilated gland.
Mrs. S.R.	76	43	"	2 weeks	-
Mrs. S.S.	66	46	"	1 month	-
Mrs. A.M.	63	48	Vaginitis	8 months	-
Mrs. H.McD.	56	50	Normal	2 years	Atrophy.
Mrs. P.R.	63	42	"	1 month	-
Mrs. H.C.	58	52	"	4 months	-
Mrs. C.L.	68	40	"	2 years	-
Mrs. J.T.	59	50	Vaginitis	1 year	Atrophy.
Mrs. M.B.	53	50	Normal	2 months	-
Mrs. H.T.	62	46	"	7 years	Atrophic.
Mrs. M.S.	64	45	Vaginitis	4 months	Atrophic.
Mrs. J. McL.	55	50	Vaginitis	5 months	-
Miss E.N.	57	51	Normal	2 years	Inactive dilated gland.
Miss E.A.	68	46	"	2 months	-

Name	Age.	Age at Menopause	Condition of vagina	Duration of Bleeding	Uninvolved endometrium.
Miss S.B.	63	53	Normal	2 months	Atrophic.
Mrs. S.S.	54	42	"	8 months	-
Miss H.S.	70	50	"	3 months	Inactive dilated gland.
Mrs. A. McG.	65	42	"	4 months	-
Miss H.G.	60	49	"	8 months	-
Mrs. H.S.	58	48	"	3 years	Inactive dilated gland.
6 years previously postmenopausal bleeding - active hyperplasia.					
Mrs. R.A.	57	53	Normal	3 months	-
Mrs. E.N.	59	47	"	3 weeks	-
Mrs. A.W.	62	48	"	3 months	Inactive dilated gland.
7 years previously postmenopausal bleeding - active hyperplasia.					
Miss H.M.	58	50	Vaginitis	8 months	Inactive dilated gland.
Mrs. J.M.	60	38	Vaginitis	5 months	-
Mrs. I.G.	58	53	Normal	3 years	Fibro adenomatous polyp.
Mrs. I.B.	61	40	"	4 months	Atrophy.
Miss M. McC.	67	50	"	3 months	-
Mrs. V.Y.	54	48	"	1 year	-
Mrs. H.R.	74	46	"	3 months	Inactive dilated gland.
Mrs. H.C.	53	50	"	10 months	-
Mrs. E. McD.	62	50	"	4 months	-
Mrs. W.S.	68	42	"	2 weeks	Inactive dilated gland.
Mrs. L.A.	75	50	Vaginitis	4 weeks	-
Mrs. P.H.	62	52	Normal	8 months	Inactive dilated gland.

Name	Age	Age at Menopause	Condition of Vagina.	Duration of Bleeding	Uninvolved endometrium.
Mrs. W.S.	52	49	Normal	9 months	Inactive dilated gland.
Mrs. H.P.	48	44	"	2 years	Active hyperplasia.
Mrs. H. McL.	70	49	"	3 weeks	-
Mrs. W.A.	65	48	Vaginitis	3 months	Atrophic.
Mrs. I. McG.	58	51	Normal	4 weeks	Inactive dilated gland.
Mrs. H.L.	55	48	"	4 months	-
Mrs. B.A.	60	39	"	3 months	Atrophic.
Mrs. E.L.	75	40	"	5 months	-
Mrs. I.B.	58	50	Vaginitis	1 month	Inactive dilated gland.
Mrs. A.G.	55	35	Normal	5 months	-
Mrs. S.H.	56	49	"	8 months	Atrophic.
Mrs. E.L.	58	50	"	1 year	-
Mrs. H.F.	61	51	"	3 months	-
Mrs. A.T.	57	52	"	11 months	Atrophic.
Miss J. McK.	56	49	Vaginitis	2 years	-
Mrs. M.M.	55	52	Normal	1 year	Atrophic.
Mrs. A.S.	62	52	"	11 months	-
Mrs. C. McG.	70	54	"	2 weeks	Inactive dilated gland.
Miss H.M.	60	48	"	6 months	-
Mrs. R.W.	62	42	"	3 months	Atrophic.
Mrs. H.P.	70	53	"	6 months	-
Miss I. McG.	75	40	"	1 year	Atrophic.
Mrs. E.G.	70	45	Vaginitis	4 weeks	-

Name	Age	Age at Menopause	Condition of Vagina	Duration of Bleeding	Uninvolved endometrium.
Mrs. O.L.	60	50	Normal	8 months	Inactive dilated gland.
Mrs. A.W.	58	44	"	11 months	Inactive dilated gland.
Miss H.K.	54	46	"	1½ years	-
Miss E. McH.	61	17	Vaginitis	6 weeks	-
Mrs. H.M.	65	50	Normal	1½ years	-
Mrs. J.H.	47	45	"	Doubtful	Atrophy.
(Previous curettings at time of menopause - atrophic).					
Mrs. A. McN.	57	52	Normal	2 years	Inactive dilated gland.
Mrs. H. McL.	53	42	"	2 weeks	-
Miss M. McM.	53	40	Vaginitis	3 weeks	Active hyperplasia.
Mrs. J.A.	60	50	Normal	8 months	-
Miss A.F.	70	47	"	6 months	Atrophy.
Mrs. J.S.	61	55	"	6 months	-
Mrs. C.M.	66	48	"	6 months	-
Mrs. M.M.	68	32	Vaginitis	5 months	Inactive dilated gland.
Miss C.B.	51	47	Normal	2 years	-
Miss J.M.	60	42	"	5 months	Atrophy.
Mrs. M.S.	55	47	"	2 months	-
Mrs. W.P.	61	52	"	1 month	-
Mrs. A.G.	55	50	"	3 weeks	Inactive dilated gland.
Mrs. J.B.	53	49	"	9 months	Inactive dilated gland.
Mrs. A.T.	60	51	"	4 months	-
Miss M.M.	50	35	"	3 days	Atrophic.

Name	Age	Age at Menopause	Condition of Vagina	Duration of Bleeding	Uninvolved endometrium.
Miss D.W.	54	40	Vaginitis	7 weeks	Inactive dilated gland.
Miss E.G.	76	50	Normal	10 months	-
Mrs. S.H.	75	45	"	2 years	-
Mrs. M.D.	66	52	"	10 months	-
Mrs. A.C.	53	46	"	2 weeks	-
Mrs. A.T.	62	55	Vaginitis	2 weeks	-
Mrs. J.H.	61	50	Normal	4 months	Inactive dilated gland.
Mrs. I.K.	54	47	"	3 months	-
Mrs. J.B.	60	50	"	8 months	-
Miss N. McK.	70	50	"	11 months	Atrophy.
Mrs. M. McP.	60	49	"	8 months	-
Mrs. G.G.	59	47	"	5 weeks	Active hyperplasia.
Mrs. M.McB.	58	55	"	5 months	Atrophic.
Miss H.P.	63	43	"	8 months	Active hyperplasia.
Mrs. L.A.	52	45	"	4 months	-
Mrs. I.M.	64	47	"	10 months	-
Miss M. McK.	72	51	Vaginitis	8 months	Inactive dilated gland.
Miss J.S.	59	49	Normal	6 months	-
Mrs. C.M.	63	52	"	4 weeks	Atrophy.
Mrs. M. McK.	63	53	"	2 weeks	-
Previous curettage - inactive dilated gland pattern.					
Mrs. M.B.	58	53	Normal	11 months	-
Mrs. B.R.	49	47	"	3 months	Inactive dilated gland.

Name	Age	Age at Menopause	Condition of Vagina	Duration of Bleeding	Uninvolved endometrium.
Mrs. M.P.	70	50	Normal	10 months	-
Mrs. J.D.	55	49	Vaginitis	5 months	Atrophy.
Mrs. E.H.	57	50	Normal	8 months	-
Mrs. J.P.	62	52	"	4 months	Inactive dilated gland.
Mrs. C.S.	53	48	"	10 months	Atrophic.