POSTMENOPAUSAL BLEEDING—ONE HOSPITAL—ONE YEAR

by

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Introduction

Post menopausal bleeding (P.M.B.) is one of the most important symptoms with which we deal in gynaecology, because of its relation to the presence of malignancy.

The literature up to 1941, reveals an alarmingly high proportion of malignant to benign causes of post menopausal bleeding. Although most recent publications have shown a falling incidence of P.M.B. due to malignancy, there still exists however, a great variation in reported series by different Authors (Table I).

This study was undertaken to determine:

(I) The incidence of malignancy in patients with post-menopausal bleeding in this Hospital.

(II) Whether the rate of malignancy in this area reflects the trends noted in other centres.

(III) Whether, in view of long waiting lists, the emergency admission of these patients is justifiable.

We feel that it is important that such studies be made from time to time, because changing factors alter the figures and a reappraisal of our opinion concern-

TABLE I

Incidence of Malignancy in P.M.B. reported by various authors

Authors	Years	No. of cases	Per cent Malignancies
Kantor and Klawans	1932	98	68.4
Geist and Matus	1133	182	57.5
Taylor and Miller	1938	406	63
Geiger	1941	395	81
Check and Davis	1946	514	36.1
Brewer and Miller	1954	222	26.6
Payne and Wright	1959	698	30
Klingenberg and Klausen	1963	—	16.1
Hammonda	1966	92	5.3
Benzie	1967	132	48
Prokope	1971	1085	28
Keirse	1973	160	23.7
Gambrell	1974	363	3

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TABLE II

	Causes of Menopausal Bleeding	Age Groups					Age at menopause (in years)			Duration of Amenorrhoea before bleeding (in years)			Parity			Total			
		Less than 50	50-54	55-59	60-64	65 and over	Less than 45	45-50	51 and over	1-2	2-5	Over 5	Nulliparous	Para 1 or 2	Para 3 and more	No.	%	Average age in years	
Malignant Lesions	Endometrial carcinoma	—	—	3	2	9	2	7	5	—	—	14	5	7	2	14	9.2	65	
	Cervical carcinoma	—	3	1	1	2	2	4	1	1	1	5	1	3	3	7	4.6	62	22(14.5)
	Cystadeno-carcinoma	—	1	—	—	—	—	1	—	1	—	—	1	—	—	1	0.7	54	
Benign Lesions	Brenner Tumor	—	—	—	—	1	—	—	1	—	—	1	—	—	1	1	0.7	67	
	Benign cervical Lesion	6	14	9	6	8	6	22	15	17	5	21	7	21	15	43	28.2	56	
	Senile Vaginitis	2	2	11	8	6	3	13	13	3	4	22	5	18	6	29	19.0	60	
	Endometrial polyp or Hyperplasia	6	9	5	1	1	2	10	10	15	3	4	2	14	6	22	14.5	54	102(67.1)
	Bleeding Urethral from the Carucle	—	—	—	2	4	1	2	3	—	—	6	—	3	3	6	4.0	66	
	Urinary Bladder Track Pupiloma	—	—	—	—	1	—	—	1	—	—	1	1	—	—	1	0.7		
	Cause not demonstrated	3	13	8	2	2	4	16	8	9	10	9	2	14	12	28	18.4	54.5	28/18.4
	No.	17	42	37	22	34	20	75	57	46	23	83	24	80	48	152	100		
	TOTAL %	11.2	27.6	24.3	14.5	22.4	13.2	49.3	37.5	30.2	15.2	54.6	15.8	52.6	31.6	100	—		

ing the clinical significance of bleeding after the menopause is essential, particularly as it related to the presence of malignancy. In this study, post menopausal bleeding is defined as the onset of any staining or bleeding from the female genital tract a year or more after the last menstruation.

Material and Methods

The records of 152 patients with post-menopausal bleeding (P.M.B.) who were admitted to Stepping Hill Hospital, during the year 1972, were studied.

These patients were coming from an area with a mixed population of 350,000 and represented 5.5 per cent of the total 2755 admissions to the gynaecological department during the period of our study. The age range was from 43 to 89 with the majority of them (52 per cent) between 50 and 60 years of age. The mean age at the time of menopause was 49.2 years with 20 women (13.9 per cent) whose periods stopped before the age of 45 and 11 women who were 54 years of age or older, when menstruation ceased. The earliest menopause occurred in a nulliparous woman at the age of 39, whilst the oldest patient at the menopause was also nulliparous woman, 59 years old with a Brenner Tumor.

We had adopted the policy that all patients with post-menopausal bleeding were admitted to the Hospital for investigation and diagnosis of the cause of bleeding. Each patient was evaluated with a minimum of a Pap test, pelvic examination, biopsy of any cervical lesion and dilatation and curettage under anaesthesia. Special investigations were done when necessary.

Results

The incidence of the various causes of P.M.B. in the 152 patients in relation to age, parity, age at menopause and duration of amenorrhoea before bleeding occurred is listed in Table II.

The patients were divided into three major groups according to the causes of bleeding,

(I) Those with a malignant lesion

(II) Those with a benign lesion

(III) Those in whom the cause for the bleeding was uncertain.

In the first two groups, physical lesions were considered the cause of the bleeding. The last group consists of those patients in whom complete investigation revealed no definite reason for the bleeding. The cause of bleeding was found to be malignant in 22 (14.5 per cent) patients, benign in 102 (67.1 per cent) and no cause for it was demonstrated in 28 (19.2 per cent) of the patients.

The mean age of patients with malignancy was 63.4 years, compared to 57 years for those with non-malignant lesions. No correlation was found between the age of menopause and the cause of post-menopausal bleeding (Table II). The majority of patients (54.6 per cent) had more than 5 years of amenorrhoea before bleeding occurred. The mean period of amenorrhoea for the entire group was 8.8 years (non-malignant 7.5 years, malignant 15.4 years). Age of menopause seems to have no apparent relation to parity (Table III).

TABLE III

Average Age of Menopause in Relation to Party (in Years)

Nulliparous	Para 1, 2	Para 3 or more
47.7	49.8	49.2

There are 7 squamous cell carcinomas of the cervix and 14 cancers of body of the uterus a rate of 1:2. In 1 case, with

clinical evidence of malignancy confirmed by biopsy, the cervical smear report was normal. Of the patients with endometrial Carcinoma one had had two curettages in two months for persistent bleeding. Her first histology report on 23-3-1970 was: "Polypoidal tissue composed of hypertrophic acini, many showing secretory function. No evidence of malignancy". Repeat curettage 13-4-1970: "No curettings were obtained". Six months later, a total hysterectomy was performed for persistent bleeding and a well differentiated corporeal adenocarcinoma was found.

In another case, curettage was performed and the histology report read as follows: "The endometrial glands show marked hyperplasia. Carcinomatous features not recognised". The bleleding recurred and she was re-admitted 9 months later for repeat curettage. The histology report read: "A well differentiated corporeal adenocarcinoma". There were 2 ovarian tumours, 1 cyst-adenocarcinoma and 1 Brenner tumour. The patient with the Brenner tumour was 67 years old, nulliparous with menopause at 59 years of age.

In the 102 cases, where the cause of the bleeding was considered to be benign, the commonest cause was benign cervical lesions followed by post-menopausal vaginitis. In 6 patients the bleeding arose from the urinary tract which should never be forgotten in investigation of this symptom. In 58 of those with a benign lesion no curettings or insufficient tissue were obtained. Of the remainder, 16 had a hyperplastic endometrium and the others atrophic post-menopausal endometrium.

There were 28 patients in whom no pathological explanation for the bleeding was found, despite a complete examination having been made. In 17 of them no tissue was obtained on curettage. The rest showed an atrophic post-menopausal endometrium. The histological structure of the endometrium in our 152 women with post menopausal bleeding, is listed in Table IV.

TABLE IV

Type of Endometrium	Number of cases				
	Malignant Lesion	Benign Lesion	No demonstrable Lesion	Total	
				No.	%
1. Nil	6	58	17	81	53.3
2. Malignant	14	—	—	15	9.8
3. Secretory	1	—	—	1	0.7
4. Poliferative	—	1	—	1	0.7
5. Hyperplastic	—	16	—	16	10.5
6. Polyp	—	9	—	9	5.9
7. Atrophic	—	18	11	29	19.1
	22	102	28	152	100%
Per cent	14.5%	67.1%	18.4%		

In the endometrial cancer group, six patients (42.8 per cent) were classed as obese as compared to 22 patients (16 per cent) in the group of 130 patients with no malignant lesion.

The incidence of associated hyperten-

sion (diastolic pressure of 100 mm.Hg. or above) in both these groups was similar (25.5 per cent and 24.6 per cent respectively). There was one patient with clinical diabetes mellitus in the endometrial carcinoma group and there were 3 in the non-malignant groups. The small number of cases does not permit any conclusion.

Discussion

Several studies have shown that the clinical significance of post-menopausal bleeding has changed in the last 30 years. It has been suggested (Hamouda, 1966, Benzie, 1967) that the differences in the incidence of malignancy in various series could be due to geographical or raciol factors. Beyond these considerations we feel that the main factors in the changes of the rate of malignancy have been,

(I) An increasing understanding of the danger of P.M.B. on the part of the patients who seek prompt medical care.

(II) Pysicians are currently more alert to this symptom and send their patients in sooner.

(III) The increasing use of oestrogen replacement therapy.

(IV) The inconsistent use of terminology and the different character of the Hospitals.

In the present study, the rate of malignancy was 14.5 per cent. This is about the same as that reported by Stoll (1949, 14 per cent) and Klingenbery and Klausen (1963, 16.1 per cent) but lower than the mean which Kraubold (1962, 48.7 per cent) arrived at, in his review of 26,157 cases in the literature and Procope (1971, 28 per cent) and Keirse (1973, 23.7 per cent) and higher than that reported by Hamouda (1966, 5.3 per cent) and Gambrell (1974, 3 per cent).

The low incidence of malignancy in our series may be attributed mainly to the early investigation without selection of all patients with post-menopausal bleeding and to the composition of the population studied. The most common malignant lesions are endometrial or cervical carcinomas with cervical carcinoma less frequent as patients with this lesion are generally younger. Of the malignancies, 86 per cent, occurred in women with interval of amenorrhoea over 5 years. This is in agreement with the previous reported observation that the incidence of malignancy in P.M.B. rises with increasing age at the time of examination. In contrast to this, Payne *et al* (1959) found a high rate of malignancy in the early post-menopausal period; 17 per cent of those in whom there had been only 6 to 12 months amenorrhoea before the bleeding, had cancer.

Contrary to other reports, in groups divided according to age at menopause there was apparently no real difference in the incidence of malignancy. In 2 cases with cancer of the uterine body, menstruation had stopped before the age of 45.

In this report, pregnancy seemed to reduce the incidence of future endometrial malignancy, as 21 per cent of nulliparous women with P.M.B. had cancer compared with 7 per cent in parous women.

In our study we were able to show a significant link between endometrial cancer and obesity; we have not been able to confirm any association with hypertension or clinical diabetes. This is in agreement with findings of Macmahon (1974), who in a controlled study was able to demonstrate an association between endometrial cancer and obesity but not with hypertension.

Hemsel *et al* (1974) have shown that in obese women the peripheral conversion of Δ 4 androstenedione to eostrone is increased. There is also some evidence that

unopposed action or excessive production of oestrone may play an important aetiological role in endometrial carcinoma (MacDonald and Siiteri, 1974). With this data we can now begin to understand how the clinically recognised predisposing factors known for many years such as obesity, liver disease and infertility can lead to post-menopausal bleeding and thus how they are related to endometrial cancer.

The conflicting results reported by different authors regarding the association between corporeal cancer and carbohydrate intolerance (Dunn *et al*, 1968) may be explained by the fact that carbohydrate tolerance can be distributed by different factors, including genetic factors, obesity and circulating oestrogen levels. Therefore, the abnormal glucose tolerance in patients with cancer of the uterine body is probably due to some factor other than the prediabetic state.

The incidence of "Causes not determined" (18.4 per cent) obtained in this study of post-menopausal bleeding is lower than in the series of Brewer and Miller (1953, 38.4 per cent) but higher than reported by other authors (0.0 to 8.8 per cent). This may be explained in part by the fact that atrophic endometrium has not been included in our study as a cause "per se" of the bleeding as other authors have done. No doubt this group included some instances of delayed menstruation. In 17 out of those 28 patients, no endometrium was obtained by curettage and in another 11 the endometrium was atrophic.

Once again, this study shows that curettage is not infallible in establishing the presence or absence of endometrial cancer, although it is so considered by some clinicians. Others regard it as so unreliable that they carry out hysterectomy in all cases where no acceptable explanation can be found. In 1 case with uterine cancer, repeated curettage failed to provide the diagnosis and caused delay of several months in the recognition of the disease. The development also of cancer in 1 patient with endometrial hyperplasia several months after the curettage emphasises the significance of recurrent bleeding at this age and the need for repeated detailed investigation and possibly hysterectomy.

The post menopausal endometrium does not always show a simple atrophic pattern; it often exhibits an oestrogen effect varying in degree (Novac, 1944, Noer, 1961, Procopes, 1968). These endometrial changes may result in uterine bleeding.

In approximately half of the patients no curettings or insufficient material was obtained, in 19.1 per cent atrophic endometrium was obtained, while in 16 patients the endometrium was hyperplastic (10.5 per cent). Although endometrial hyperplasia may occur from the effect of oestrogen secreted by re-awakening ovarian function, or by the peripheral conversion of androgen (mainly Δ 4 androstenedione) to oestrone, it is often produced by the administration of oestrogen to relieve menopausal symptoms. In this series, only 8 patients had received some form of oestrogen therapy prior to the bleeding. None of the 8 cases was found to have genital cancer. This is surprisingly low incidence (5.2 per cent) especially when compared with the series reported from the U.S.A. (Payne, 1959, 8 per cent; Gambrell, 1974, 46 per cent). This probably reflects the attitude of the profession in this area towards the administration of exogenous oestrogen to women at the menopause.

The duration, quantity or character of

the bleeding, does not help us to distinguish malignant from benign lesions. Therefore, in cases of post-menopausal bleeding the cause of the bleeding must always be ascertained by curettage.

Conclusions

Although the incidence of post-menopausal bleeding due to malignancy has fallen, it remains sufficiently high to require immediate and thorough investigation. The incidence of a malignant cause of P.M.B. increases, as the time lapse between the menopause and onset of bleeding increases. Nulliparity and obesity constitute high risk factors for endometrial carcinoma.

Summary

During a one-year period, the causes of post-menopausal bleeding in 152 women were studied. The time lapse from the last menstruation was one or more years.

The cause of bleeding was found to be malignant lesion in 22 women (14.5 per cent), a benign lesion in 102 (67.7 per cent) and undetermined in 28 (18.4 per cent).

Adenocarcinoma of the endometrium was found in 14 patients (9.2 per cent) with squamous cell carcinoma of the cervix accounting for 4.6 per cent of the causes of bleeding. Approximately 86 per cent of malignant disease occurred in women with an interval of amenorrhoea exceeding 5 years and the incidence of genital cancer increased with the age of the patient at the time of examination. Of the multi-parous women with post menopausal bleeding, 21 per cent had an endometrial carcinoma compared with 7 per cent of the parous women. Endometrial adenocarcinoma was also shown to be associated unduly frequently with obesity but we have not been able to confirm any association with diabetes mellitus, as is frequently stated, nor with hypertension.

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References

1. Benzie, R. J.: Aust. N. Z. J. Obstet. Gynec. 7: 73, 1967.
2. Brewer, J. J. and Miller, W. H.: Am. J. Obstet. Gynec. 67: 988, 1954.
3. Brown, R. (1974b): Journal of Obstet. and Gynec. of the British Commonwealth. 81: 940-946, 1974b.
4. Check, D. B. and Davis, J. E.: Am. J. Obstet. Gynec. 52: 756, 1946.
5. Dunn, L. J., Merchant, J. A., Bradbury, J. T. and Stone, D. B.: Archives of Internal Medicine. 121: 246, 1968.
6. Gambrell, R. D.: J. Am. Ger. Society. 22: 337, 1974.
7. Geiger, G. J.: Illinois Med. J. 80: 406, 1941.
8. Geist, S. H. and Matus, M.: Am. J. Obstet. Gynec. 25: 388, 1933.
9. Hamouda, A. A.: Aust. N. Z. J. Obstet. Gynec. 6: 190, 1966.
10. Hemsell, D. L., Siiteri, P. K. and MacDonald, P. C.: J. Clin. Endocrinol. 38: 476, 1974.
11. Kantor, A. E. and Klawans, A. H.: Am. J. Obstet. Gynec. 24: 1972, 1932.
12. Keirse, M. J. N. C.: Postgraduate Medical Journal. 49: 344, 1973.
13. Klingenberg, I. and Klausen, H. K.: T. Norske Laegeforen. 85: 534, 1963.
14. Kraubold, E. D.: zbl Gynak. 85: 1242, 1962.
15. MacDonald, P. C. and Siiteri, P. K.: Gynecologic Oncology. 2: 259, 1974.

16. MacMahon, B.: Gynecologic Oncology. 2: 122, 1974.
17. Novak, E.: J. Clin. Endocrinol. 4: 575, 1944.
18. Payne, F. O. nad Wright, R. C. and Fetterman, H. H.: Am. J. Obstet. Gynec. 77: 1216, 1969.
19. Procope, B. J.: Acta. Endocrinol. 60: Suppl. 135, 1968.
20. Procope, B. J.: Acta. Obstet. Gynec. Scand. 50: 311, 1971.
21. Stoll, B.: Med. Klin. 44: 564, 1949.
22. Taylor, H. and Miller, R.: Am. J. Obstet. Gynec. 36: 22, 1938.