

Post-menopausal smear patterns – A review of vaginal smears in 480 women

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Summary

Cytohormonal evaluation was done on the vaginal smears of 480 normal, asymptomatic, post-menopausal women whose ages ranged from 36 to 74 years. About 50% showed atrophic smears consistent with total oestrogen lack. 41% had mild to moderately proliferative smears compatible with sub-optimal oestrogen stimulus. 9% showed a highly proliferative pattern typical of unopposed oestrogen effect and in this group two women had atypical endometrial cells in their smears, which subsequently were found to come from an atypical endometrial hyperplasia and an endometrial adenocarcinoma-in-situ. The clinical relevance of cytohormonal studies in post-menopausal women is briefly discussed.

Keywords: Cytohormonal evaluation, vaginal smear patterns, post-menopausal.

Introduction

The endocrine turbulence that generally characterises the pre-menopausal phase of a woman's life, gradually settles into menopause with the concomitant decline of ovarian function. Vaginal cytology has long been recognized as an eminently suitable and highly sensitive method for assessing the hormonal status of a woman. Cytological interpretation of hormone effects is based on the thickness and maturation of the vaginal mucosa, which are dependent on the type and concentration of circulating sex hormones. In the total absence of hormonal stimulation, the vaginal squamous epithelium is thin and atrophic and is composed of the basal layer with a few, usually two to five, layers of parabasal cells. When oestrogen is present in optimal amounts the epithelium proliferates to its maximum thickness. The vaginal epithelium then has several layers of intermediate cells above the parabasal cells and over the intermediate cells there are a few rows of superficial cells. An atrophic smear is made up entirely of parabasal cells, whereas a smear taken at peak oestrogen activity will show a predominance of superficial cells. The interpretation of a smear composed entirely of intermediate cells is more complex since a variety of situations may be responsible for this — sub-optimum oestrogen stimulation, pure progestational or androgen effect or a combined oestrogen progesterone stimulus.

This project was undertaken to determine the cytohormonal patterns in 480 normal, asymptomatic, post-menopausal women and ascertain their clinical relevance.

Since this was a retrospective study from material submitted primarily for cervical cancer screening and not a correlative cyto-hormonal evaluation, no FSH, LH or oestrogen values are available for any of the women comprising this group.

Materials and methods

480 smears submitted for routine cervical cancer screening from women clinically evaluated as post-menopausal were included in the study. At least one year had elapsed since the onset of menopause and relevant data, particularly date of last menstrual period and gynaecological history were available in all the cases, which came from the Maternity Hospital, Kuala Lumpur, Kuantan General Hospital and several Health Centres in Johore. None had any gynaecological symptoms.

Cytohormonal assessment was done on vaginal smears and on the vaginal component of VCE smears (vaginal/cervical/endocervical), stained by the standard Papanicolaou method and found free from inflammatory changes or other abnormalities.

A smear was classed as atrophic if only parabasal cells were encountered (Fig.1), mildly proliferative if both parabasal cells and intermediate cells were present (Fig.2), moderately proliferative if the smear was almost entirely made up of intermediate cells (Fig.3) and highly proliferative if superficial cells formed the predominant epithelial component (Fig.4).

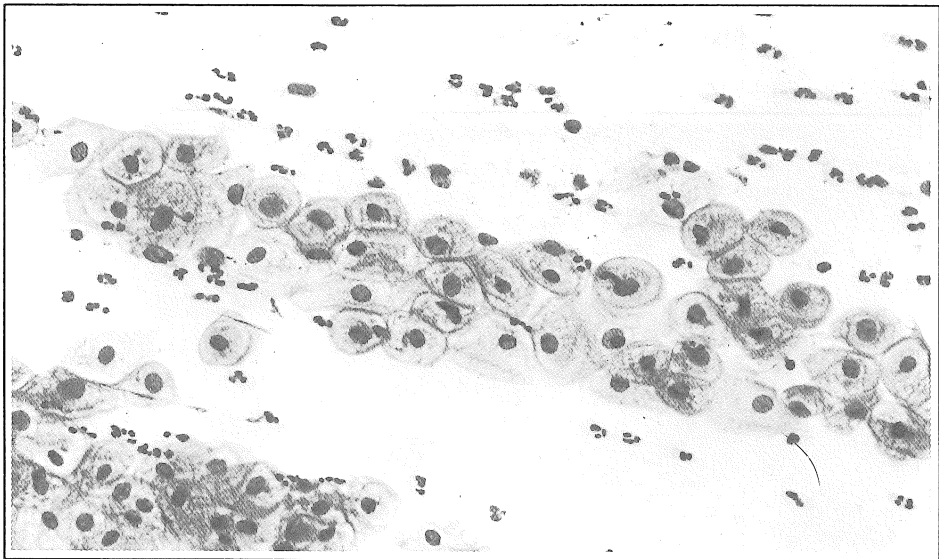


Fig. 1 : Atrophic smear (PAP stain x 20)

Results

The youngest woman in the group was 36 years old while the oldest was 74.

44.3% were between 51-70 years but the majority, (33.5%) of patients were between the ages of 56 and 65.

The duration of menopause varied from 1.5 years to 31 years. Though the proportion of atrophic smears increased steadily with advancing years, a small but significant number of women showed markedly proliferative patterns that persisted far into old age.

Moderately proliferative smears were highest in those between 35-50 years, while mildly proliferative patterns were seen in a wider age group, namely 35-60 years.

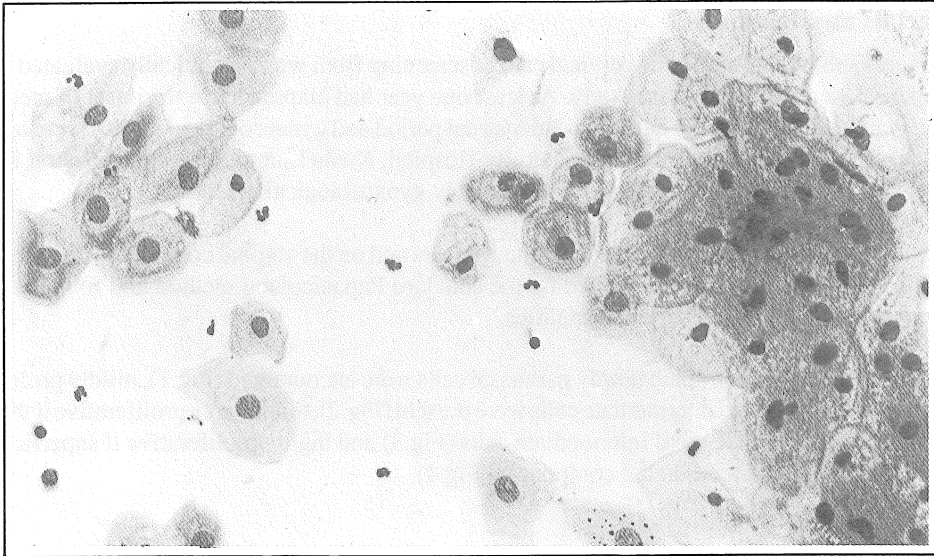


Fig. 2 : Mildly proliferative smear (PAP stain x 20)

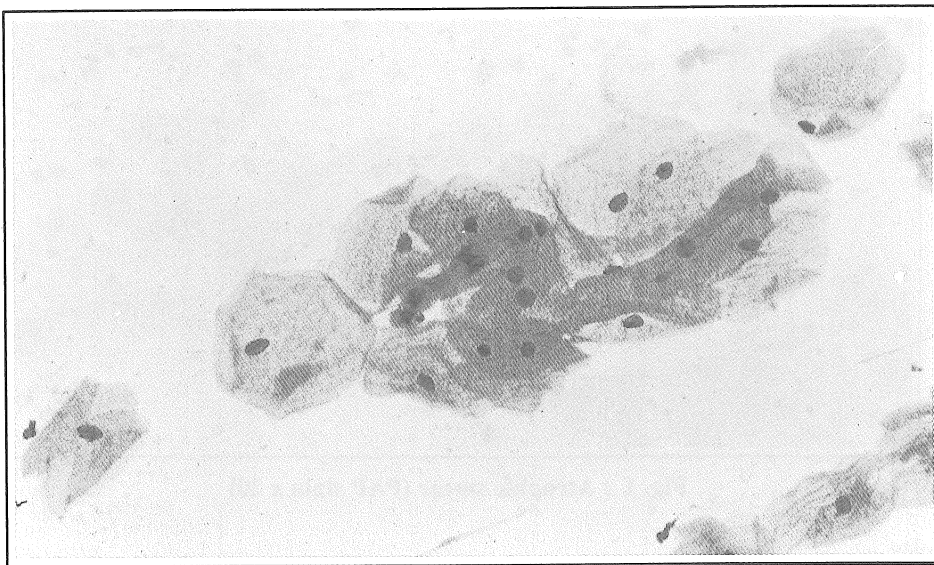


Fig. 3 : Moderately proliferative smear (PAP stain x 20)

The findings are summarised in Tables I and II.

Two women, one 58 years old and four years since menopause and the other 62 years old and eight years since menopause had highly proliferative smears with a typical endometrial cells. The presence of these cells necessitated further investigations and endometrial curettage at a later date revealed a typical endometrial hyperplasia in the first patient and adenocarcinoma-in-situ in the second.

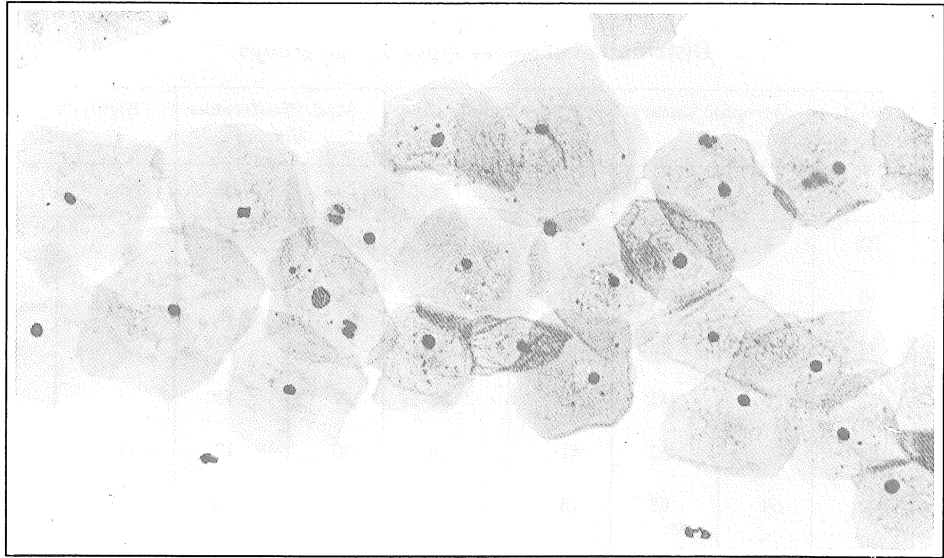
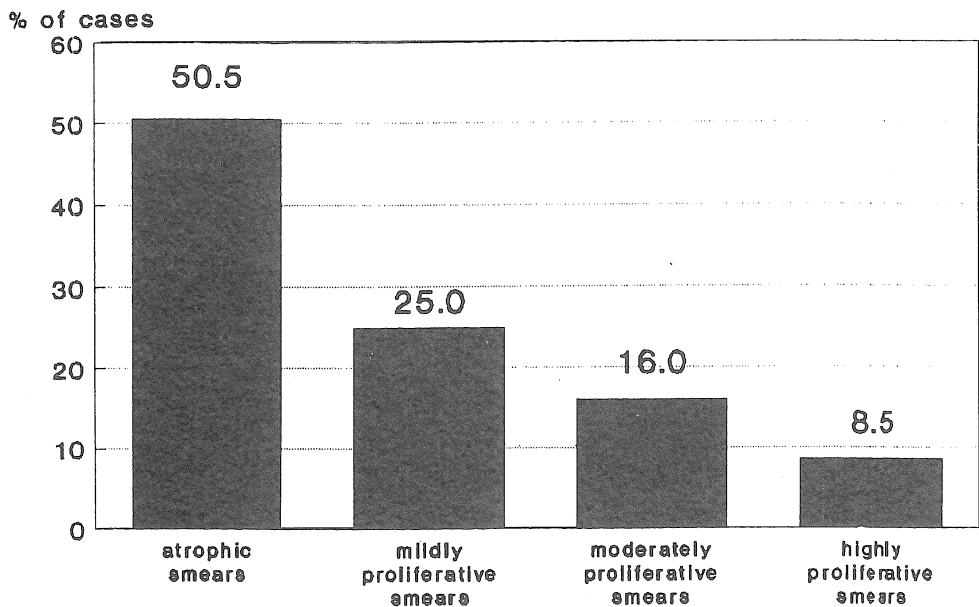


Fig. 4 : Highly proliferative smear (PAP stain x 20)

Table I : Distribution of Post-menopausal smear types (%)



Discussion

Vaginal Cytology is a rapid, painless, inexpensive and reliable method of assessing hormonal status, practised since Papanicolaou and Shorr's¹ publication on the subject in 1936. Though urinary and blood oestrogen estimations are easily performed now, they are expensive, time-consuming and generally available only in big centres. Moreover, there is some doubt as to whether they are reliable indicators of end-organ effect, which is well known to vary greatly in response to the female hormones.

Table II
Distribution of smear types by age groups

Age Group (yrs)	Total No. of Cases	Atrophic Smears		Mildly Proliferative Smears		Mod. Proliferative Smears		Highly Proliferative Smears	
		No	%	No	%	No	%	No	%
35-40	20	3	15	9	45	5	25	3	15
41-45	30	6	20	10	33	9	30	5	17
46-50	34	9	26	10	29	8	24	7	21
51-55	62	26	42	20	32	9	15	7	11
56-60	174	92	52	41	24	30	17	11	7
61-65	102	69	68	18	17	10	10	5	5
66-70	40	26	65	8	20	4	10	2	5
71-75	18	11	62	4	22	2	11	1	5

The vaginal epithelium is considered to be the most sensitive indicator of oestrogen effect, of all hormone responsive tissues in the body.² Though this study has not attempted to correlate smear patterns with symptoms or the several physical, psychological and social problems associated with the menopausal state, it shows clearly that hormone production does not halt abruptly with the onset of menopause.

Only about 50% of women showed total oestrogen lack, while the rest had smears indicative of some type of hormonal stimulus, which in the highly proliferative smears was compatible with peak oestrogen activity. The source of this oestrogen has been the subject of much study and speculation. Oestradiol, produced in a cyclical fashion by the ovaries in the reproductive phase, decreases in amount in the pre-menopausal woman. Oestrone, on the other hand is still present in the post-menopausal woman and is now thought to be produced by the conversion of adrenal cortical androstenedione in the peripheral tissues, particularly adipose tissue.³ In support of this Saez et al⁴ have shown plasma oestrone levels that are similar in post-menopausal women who have and who have not undergone oophorectomy.

While endogenous oestrone production, a greatly variable activity, may explain the erratic oestrogenic effects observed in the years following menopause, other possibilities may have to be borne in mind. Oestrogenic effects of certain foods like soya flour and linseed⁵, residual oestrogens in meat from chicken and cattle fattened by stilboestrol and oestrogens absorbed by the skin from cosmetics⁶ have been reported. Tetracyclines⁷ and digitalis⁸ have been known to produce a proliferative effect on the vaginal epithelium.

The results of this study are comparable with those of earlier studies^{9,10} - 50% of women showing negligible oestrogen effect, 41% showing mild to moderate oestrogenic activity and 9% showing a high degree of oestrogenic stimulation.

The clinical implications of these findings are worthy of note. Firstly, age at onset of menopause and duration of menopause have no correlation with the hormonal status as observed from the vaginal cytology - totally atrophic smears were seen in the below 40 group with duration of menopause less than three years, while proliferative smears were noted in women over 70 with duration of menopause over 20 years.

Secondly, selection of cases for hormonal replacement therapy should preferably be done after a full clinical and cytohormonal evaluation, to avoid indiscriminate use of oestrogens and its attendant complications. In this context, younger women who show severe oestrogen lack at an early phase of menopause may have a higher risk for osteoporosis and should be considered for early oestrogen substitution.¹¹

Another pertinent implication is the significantly higher risk of endometrial carcinoma and cervical carcinoma in post-menopausal women with highly proliferative smears.¹² This is generally not well known and therefore follow-up with additional investigative procedures is not the usual practice. The presence of endometrial cells, however benign, at any time in the postmenopausal phase is abnormal. If this is associated with a highly proliferative smear, the cytopathologist advises curettage to detect/exclude endometrial pathology. In the absence of endometrial cells, a well oestrogenised smear calls for careful evaluation of the patient, specially if she is obese or diabetic and has no gynaecological complaints, before a diagnostic curettage is contemplated. It follows from this, that in the absence of hormone therapy or other factors known to produce proliferative patterns, (diet etc), a woman in the established postmenopausal phase, with an oestrogenic smear should be placed in the "close-follow-up" list.

Lastly, there may be a place for cytohormonal assessment in monitoring optimum dosage for women who are going to be supplemented with oestrogens.

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