

POPULATION SCREENING FOR CANCER OF THE FEMALE GENITAL TRACT

by

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There is no invasive cancer which at one stage was perhaps not cancer-in-situ. The cervical lesion, if detected at its preinvasive stage, or better still, at the stage when cervical epithelium is showing precancerous dysplastic changes, is amenable to treatment by surgery and/or radiation. Patients treated at preinvasive stage have a 100 per cent survival rate after 5 year follow-up (Te-Linde 1952, Kottmeier, 1953). This is in marked contrast to the very low survival rate among patients during the advanced invasive stage. It is thus imperative to diagnose symptomless cervical carcinoma which is invariably negative for any gross pathology in cervical epithelium. To control the disease the diagnosis has to be made in the curable stage when the carcinoma is non-invasive, usually asymptomatic and presents no visible alterations in the appearance of cervical mucous membrane. Prophylactic examination of apparently well women without any complaints is thus essential to secure the early detection of cancer and pre-cancer.

Screening of women for early detection of cancer, preferably in its

preinvasive stage is receiving widespread attention. The successful application of the study of exfoliated cells in the detection of incipient or hidden carcinoma of the uterine cervix and other organs has made this technique particularly suitable for mass screening in cancer detection.

In western countries cytology has helped preventive medicine to score victory over cancer. Ayer (1961) in a recent editorial on cancer cytology has correctly emphasized that "today cytology will detect cancer of cervix early enough to render it a preventable disease. Cytology is a revolutionary prediagnostic screening system which should be used on all women. Ninety per cent of preinvasive cancer are totally unsuspected and such early cancers are hundred per cent curable." Shimkin's statement at the Fourth National Cancer Conference (USA) is worth a careful study. "If every woman in this country could be studied by cytology every year or two, 9 out of 10 deaths from cervical cancer could be prevented. The difficulty is that though we know this, far too many physicians cannot be persuaded to use cytology routinely. So long as there are women who need and want this type of protection but cannot get it from the doctors, there will be a need

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and a justification for large community screening programmes."

Wahi and Mali (1962) reported findings of a mass detection programme in Indian women wherein they detected 74 cases of positive vaginal cytology in the clinically unsuspected women under 30 years of age, with the possibility of one hundred per cent cure. They also found cytological screening to be an excellent technique for the study of epidemiology of cancer in this country. The morbidity data from cases confirmed by cytologic examination should prove considerably more useful than currently available figures which rely almost exclusively on mortality figures. Cancer detection clinics should be organised to use cytology as a mass screening procedure and such a programme will permit a unique opportunity for the study of progression of cancer through its earliest stages—a stage when the host environment has not had time to be altered by the advancing disease.

Methods and Material

The results of this study are based on the examination of 44,919 vaginal smears in 39,587 women over a period of 3 years. No attempt at selection on any basis was made. A detailed clinical and vaginal examination was done in every case and vaginal and cervical smears were collected as a screening procedure. Smears were obtained by means of vaginal pipette from the posterior fornix pool and cervical scrapings were collected by means of Ayer's wooden spatula. The smears were stained according to the Papanicolaou's technique.

The smears were read and grouped on cyto-morphological basis as follows (Kehar and Wahi, 1965):

Group I	: Absence of atypical or abnormal cells.
Group II	: Atypical cells showing mild (Grade I) dysplastic changes.
Group III	: Atypical cells showing moderate (Grade II) dysplastic changes.
Group IV	: Atypical cells showing marked (Grade III) dysplastic changes.
Group V	: Cytology conclusive of malignancy.

Patients with group 1 smear were not followed up. Those with group II and group III smears were studied again regardless of their pelvic abnormality. It is important to emphasize the fact that to increase the accuracy of the screening technique, all women who had smears classified as group II were requested to have further cytological study. An attempt was made to observe closely the patients with group II smears by examination of smears every 3 months. Patients persistently having group III smears with or without observable cervical lesions were subjected to cervical biopsy. Similarly all patients with group IV or group V smears were subjected to the surgical diagnostic procedure.

Cytological examination in spite of its being a diagnostic tool based on sound morphological principles, has certain limitations and the following would be found to be a sound guiding principle. A smear is a screening procedure and a report of a suspicious or positive smear is an opinion only and should serve to initiate further diagnostic procedure. Con-

firmation of cytologic observation by biopsy is strongly recommended before the institution of therapy.

Observations and Comments

The following table gives the cytological findings in the total number of women examined.

TABLE I

Cytologic findings in 39,587 women

Type of smear	No. of cases
Malignant	693
Dysplastic	927
Unsatisfactory	868
Negative	37,099
Total	39,587

Among 39,587 cases examined cytologically, 693 cases showed the presence of malignant cells giving an incidence of malignancy as 17/1000 cases examined.

The yield of various screening programmes expressed as rate of diagnosing cancer cases per 1000 women examination has varied considerably.

TABLE II

Incidence of cervical carcinoma as reported by different workers

Authors	Incidence/1000
Kimmelsteil (1954)	5.7
Day (1956)	3.0
Soule (1956)	7.5
Erickson (1957)	5.8
Stevenson (1962)	5.0
Christopherson (1962)	13.0
Macgregor (1963)	10.0
Schonberg (1965)	23.0
Present study (1965)	17.0

These differences in results probably reflect variations in epidemiological factors, such as age, parity, social status and ethnic background of the screened population (Jones, 1958).

Age

The following table shows the ages of the women with positive cytology:

TABLE III
Age at diagnosis in 693 cases of carcinoma

Age group in years	No. of cases
14 and below	Nil
15-20	4
21-26	18
27-32	76
33-38	103
39-44	131
45-50	231
51-56	54
57-62	56
63 and over	20
Total	693

The youngest patient with cancer of cervix was 18 years old and the oldest patient's age was 80 years. It is interesting to note that four patients with carcinoma were less than 20 years of age. This finding confirms the view that if deaths from cancer have to be eliminated, the disease must be diagnosed in the early stages by application of cytological test to all women over 20 years of age, and to those younger ones who have been pregnant or married (Ferguson, 1961; Lund, 1961; Nieburgs, 1956; Wahi, 1962).

Presenting Symptoms

TABLE IV
Presenting symptoms in 693
cancer cases

Symptoms	No. of cases
Bleeding per vaginam	550
Discharge per vaginam	103
Pain in abdomen	23
Other gynaecological symptoms ..	17
Total	693

The commonest significant symptom, bleeding per vaginam, which leads patients to consult a doctor, raised the proportion of invasive lesions notably. If the patient went to the doctor with significant symptoms, she was approximately $2\frac{1}{2}$ to 3 times more likely to have invasive carcinoma than cancer-in-situ or a dysplastic lesion.

The above table also shows that early cases of cancer cervix seldom arouse clinical suspicions. 143 cases in this series had no significant symptoms related to cancer cervix, thereby supporting the already known fact that in the early stage cancer of cervix may be asymptomatic.

Out of 39,587 unselected women in the present series, 64 cases, clinically unsuspected for malignancy, showed the presence of malignant cells in the vaginal smears. In each of these cases initial clinical impression of the cervix was other than carcinoma (Table VI). Cytological examination furnished the first positive indication of malignancy.

TABLE VI
Clinical impression of cervix in
64 unsuspected cancer cases

Clinical impression	No. of cases
Chronic cervicitis	26
Erosion cervix	24
Healthy looking cervix	6
Prolapse uterus with ulcer	5
Cervical polyp	3
Total	64

The cervix was healthy looking in 6 cases, erosion was present in 24 cases, and 26 cases had chronic cervicitis. According to Papanicolaou's classification the exfoliated cells in all these cases belonged to group IV or V. Cytological findings were confirmed by biopsy in 48 cases.

The above findings indicate that

TABLE V
Relationship between clinical and cytological diagnosis

Cytological Diagnosis	Clinical Diagnosis						Total
	Cancer cervix	Cancer of body uterus	Cancer vagina	Cancer vulva	Other diseases	Healthy cervix	
Carcinoma ..	629	8	6	4	58	6	711
Dysplasia ..	42	0	0	0	730	155	927
Negative ..	0	0	0	0	8,777	29,158	37,935
Total ..	671	8	6	4	9,565	29,319	39,573

clinical suspicion is seldom aroused by history or physical examination of early carcinoma; 64 cases who were clinically not suspected of malignancy were diagnosed to have malignancy of uterine cervix by vaginal cytology. This is the most significant fact relating to the value of cytological diagnosis. This gives the pick-up rate as 1.62/1000. The pick-up rate of so-called unsuspected cases ranges from as low as 2/1000 to as high as 15/1000 (Langley 1960, Maclarene *et al.* 1956, Anderson 1959, Brudenell 1956, Scott 1960, Grant 1963). This wide variation in the pick-up rate might be due to the difference in selection of cases. It will be apparent that the number of unsuspected cases diagnosed is the most significant single criterion now available to us in assessing the value of this method of mass screening.

There is increasing evidence that epithelial atypias like basal-cell hyperplasia and epithelial dysplasia precede preinvasive carcinoma, (Galvin *et al.* 1952; Mackay *et al.* 1952; Peckham and Green 1957; Wheeler and Hertig, 1955; Kehar and Wahi 1965), and which after a length of time may progress to invasive carcinoma (Carter *et al.* 1956; Galvin 1952; Peterson and Hornbrook 1952; Stevenson and Scipiades 1938; Young *et al.* 1949). The length of time a preinvasive lesion exists as such is uncertain, and in some cases does appear early in life.

In order to understand more clearly the pathogenesis of cancer cervix a study of cervical dysplasia has been done. There were 927 cases which showed the presence of mild to marked degree of dysplastic changes. This lesion was present in 1 out of 40

women in a population of 39,587 cases examined; 2817 cases were pregnant and out of these 160 were associated with dysplasia of cervix. A follow-up study was possible in 117 cases only. An attempt was made to observe closely these 117 cases every 1 to 3 months, over a period of 3 years. Progression from lower grade dysplasia to higher grade of dysplasia or carcinoma was noticed in 15 cases. One case progressed from moderate to marked dysplasia and finally to preinvasive carcinoma in 4 months. One case progressed from marked dysplasia to preinvasive carcinoma in 2 months. Two cases progressed to invasive carcinoma in a period of 9 months. One case of moderate dysplasia progressed to marked dysplasia and finally to invasive carcinoma in 14 months.

On the basis of the available incidence with clinical and experimental data, these dysplastic changes could be considered to represent a stage in the process of carcinogenesis. These, therefore, warrant a careful follow-up study over a prolonged period. If these 927 cases of dysplasia are grouped with 693 cases of cancer, there is a group of 1620 cases who had either a frank cancer or were harbouring a potential cancer. Their detection in early stages would either ensure cure or prevention of cancer of uterine cervix.

Conclusions

Cytological diagnosis is one of the few break-throughs in the battle against cancer and is perhaps the most outstanding contribution to cancer control problem.

Until the time that a more specific knowledge of the cause of uterine cervix is available, efforts should be directed towards early detection in preinvasive stage, so that treatment instituted at this stage may be fruitful in reducing mortality.

The importance of early detection of cancer cervix preferably in the preinvasive stage when cure could possibly be affected is receiving widespread attention. The findings reported in this study strongly support the opinion that patient's symptoms and clinical impression of cervix offer no guidance to the presence of malignant lesions in its early phases. Cytological method of diagnosis can provide a valuable means of picking up cases of unsuspected cancer at a time when clinical evidence has not yet manifested.

The present study further indicates that the screening for cervical cancer in women should not have any age limit. Furguson's (1961) contention that, "if a girl is old enough to have a vaginal examination she is old enough to have a cervical cytological examination", should be the practical guide. If this method could be used to find out the preclinical localised cancer in large groups of apparently healthy women irrespective of their age, this technique can be applied as a screening procedure. The majority of women in such a population could then be assured that there was no evidence of uterine cancer, while the smaller group, with suspicious positive cytology should be further evaluated by another smear examination followed by biopsy. In case of non-neoplastic lesions like dysplasia of cervix, a close follow-up by repeat-

ed smear examination is done to study the ultimate fate of such an abnormality.

As cytological studies become more widely used one would expect more cancer of cervix to be detected. Eventually there should be a shift in the ratio between in-situ and invasive carcinoma discovered, the number of invasive carcinoma proportionately falling as more and more of preinvasive lesions are detected and treated. One can safely predict that if uterine cancer cell examination could be given to all adult women, loss of life from cervical cancer could be almost totally eliminated.

The death rate from cancer cervix will fall as mass screening practice prevents the development of late stages of cancer of the cervix. However, one would expect a lag of several years between screening efforts and falling death rate.

Summary

This study comprises an examination of vaginal smears of 39,587 women aged 14 to 80 years. Out of these, 693 cases showed the presence of malignancy of female genital tract, thus one out of every 57 women suffered from cervical cancer in a total population of 39,587 examined.

On cytological and histological analysis carcinoma of the cervix was detected in 64 clinically unsuspected cases. This gives a pick-up rate of 1.62/1000. In each of these cases the initial clinical impression of the cervix was other than carcinoma, the first indication of malignancy being the result of cytological examination.

Four patients of cervical carcinoma were less than 20 years of age.

In the present study there were 927 cases of cervical dysplasia. The lesion was seen in 1 out of every 40 women in a population of 39,587 cases examined. Out of these, 160 cases were pregnant at the time of examination, thus giving an incidence of cervical dysplasia associated with pregnancy as 5.68 per cent. A follow-up study was possible in 117 cases only; 2 cases of different grades of dysplasia progressed to preinvasive carcinoma and 3 cases to invasive carcinoma.

These findings strongly support the need for routine cytological examination of all young females from time to time for detection of cervical neoplastic lesions in its early stages, and a thorough follow-up of all the dysplastic lesions of the cervix.

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