

# CYTOLOGICAL CHANGES FOLLOWING IRRADIATION FOR CANCER CERVIX

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## Introduction

Until recent years surgery and irradiation have been thought of as two alternative methods of treatment of cancer cervix with little to choose in between them—especially in stage II—though some advocated surgery and others radiotherapy. For a long time gynaecologists and radiologists had an uneasy feeling that they are unable to offer a cure for this type of patients. But exact objective indices of correlation for these intuitive guesses were lacking.

Graham (1954, 1956) reported that host tissue response to irradiation can be predicted by morphological changes in normal parabasal cells, the sensitisation response (SR) and Karyopyknotic index (K.P.I.) in the pre-treatment smear. She (1947) reported that patients with high SR responded well to irradiation and those with poor SR were best treated with surgery. Conversely, when patients with poor SR were treated with irradiation and high SR patients were treated by surgery, results were poor. Since her initial work many investigators have repeated various studies on SR and clinical response but had disappointing results.

Following further studies Graham (1951, 1953, 1954) reported that patients

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with good SR showed good radiation response i.e. over 70% of benign cells showed radiation induced changes and that stage II patients with good RR had a better 5 year survival rate than those with poor RR. Many workers have confirmed these findings. Wachtel (1956) and Graham (1958) reported that persistence of high K.P.I. after irradiation indicated presence of recurrent or residual tumour.

## Material and Methods

Initially this study was planned to evaluate the relationship, if any, of clinical type of tumour, degree of anaplasia of the tumour cells and SR and response to surgery or irradiation. Majority of the patients who attended our clinic belonged to carcinoma cervix stage III at the time of initial visit. So the study really became an observation of radiation changes in benign and malignant cells and of regression/recurrence pattern of growth after irradiation.

Fifty-five women of whom only 9 belonged to stage II and rest to stage III were studied (Table I). Clinical assess-

TABLE I  
Cases Taken up for Study

(a) Cancer Cervix stage II	..	9
Treated with Surgery	..	4
Treated with irradiation	..	5
(b) Cancer Cervix stage III	..	46
(Treated with irradiation)		

ment of type and stage of growth was done and SR and degree of anaplasia of tumour were graded in the pretreatment smear. Patients submitted for irradiation were followed up by smears at weekly intervals during irradiation and up to 3 months after irradiation and later once a month. Patients submitted for surgery were followed by monthly smear examination.

#### Observation

Four patients of stage II were subjected to surgical treatment.

alive and well 2 years after Werthiem's hysterectomy.

Clinical stage in patients with high SR may be difficult due to friability of tumour tissue. The lack of fibrous tissue response in patients with high SR may allow the tumour to spread far and wide. Even after complete surgical extirpation there may not be adequate fibrous tissue reaction to strangle the stray malignant cells.

Fifty-one patients were treated with irradiation—five belonged to stage II and the rest to stage III.

TABLE II  
Sensitisation Response: Radiation Response in Patients Treated With Irradiation

S.R.	R.R.			Total
	Poor	Border line	Good	
Poor	18	3	4	25
Border line	2	7	1	10
Good	1	2	13	16
	21	12	18	51

**Case No. 1.** 60 year old patient with exophytic growth; cytology showed high SR., malignant cells were anaplastic. On opening the abdomen soft vascular friable growth was almost filling the entire pelvis and para-aortic nodes were infiltrated. Hence surgical approach was abandoned.

**Case No. 2.** 54 year old patient had an exophytic growth, SR was high and showed anaplastic malignant cells. One month after surgical extirpation, a small raw area was seen in the vault. Vaginal smear showed anaplastic malignant cells.

**Case No. 3.** 36 year old woman had endocervical carcinoma stage II late; SR was low. Malignant cells were well differentiated. Patient is alive and well with no clinical or cytological evidence of malignancy, 3 years after Werthiem's hysterectomy.

**Case No. 4.** 52 year old patient came with an endophytic growth; SR was borderline and malignant cells were differentiated. Patient is

As a result of irradiation cells in the exfoliated material show marked alteration. Typical post-irradiation smear consisted of vacuolated basal and parabasal cells and histiocytes. Shape of cells and staining characteristic varied markedly. Occasionally—gigantism—large cells with enlarged nuclei was seen (Fig. 1). The most prominent nuclear change was the folding and wrinkling of nuclear membrane, multinucleation, hyperchromasia, chromatin clumping, Karyorrhexis and pyknosis were seen. Irregular and often large perinuclear halos were seen quite frequently. "Cannibalism" was an occasional feature, both among the benign and malignant cell (Fig. 2). Multinucleated histiocytes of bizarre shapes of-

ten exhibited phagocytosis (Fig. 3). Patients with good SR had good RR and vice versa. (Table II). Malignant cells also showed these changes to a varying extent. Residual tumour after irradiation, exfoliated malignant cells which were more anaplastic. Clinical findings prior to and after irradiation were correlated with SR, RR and degree of anaplasia.

It was found that in patients with high SR and good RR the growth regressed rapidly. Vagina and parametria remained fairly unscarred and soft. Unfortunately when the tumour could not be eradicated after irradiation the residual tumour tissue grew more rapidly than the untreated one. Regression and recurrence were most rapid when the tumour was anaplastic.

Patients with low SR did not show marked regression after irradiation. Necrosis and fibrosis were dominant. Vaginal adhesions developed and parametria became rigid bands. Because of fibrosis, assessment of residual tumour tissue becomes rather difficult. Growth of residual tumour was not markedly accelerated. In our series almost all cases showed some amount of acceleration of growth rate following irradiation. The rate of growth of persistent focus seems to be directly proportional to the rate of regression with irradiation so that at the end of a given period of time e.g. 3-6 months after irradiation there was not much of a difference between responder and non-responders in clinical staging of persistent growth. This may account for the skeptical view of many investigators about the theory that there are radio sensitive and radio resistant tumours.

#### *Summary and Conclusions*

Pre and post treatment clinical and cytological data of 55 women with cancer

cervix were studied. Of these 4 had Werthiem's hysterectomy and the rest were submitted to irradiation.

The 2 patients who had high SR and exophytic tumour did not respond well to surgery.

Patients with good SR showed good radiation response. Clinically growth regressed rapidly without scarring in patients with high SR. Patients with low SR did not show marked regression after irradiation.

Rate of growth of residual tumour was proportional to the rate of regression with irradiation so that at the end of the given period of follow up, there was not much difference in the clinical stage of residual tumour between those who responded to irradiation and those who did not.

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See Figs. on Art Paper VIII

Female sterilization has become a widely practiced and acceptable procedure in our country. It is important that each a community practice operation should be safe, efficient, acceptable and should not leave behind unpleasant sequelae. These operations are now being performed on a large scale in many districts places. One of the main reasons for it is not aware of the various complications which may follow the operation as these patients will often return for their complaints. In this paper an effort is made to out-

TABLE I

Method	Total	Complications	Deaths	Survival	Yields	Labels
Abdominal	20	1	1	18	2	1
Vaginal	10	1	1	8	1	1
Total	30	2	2	26	3	2

which could not be directly related to the operation were not considered. No positive relationship between the positive and negative of complications was found. Table I shows the different methods of sterilization used in this series.