INTRODUCTION AND AIM OF WORK

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Cancer of the uterine corpus is the commonest female gynecological cancer seen today, although this has evolved through a reduction in the incidence of cervical cancer, evidence exists to support the premise that the incidence of the disease is increasing **(Oram , 1990, and Mencaglia et al., 1990).**

Any approach to the control of endometrial cancer must include a consideration of the individual at high risk . Endometrial hyperplasia has since long been proposed to be a predecessor to endometrial carcinoma **(Disaia and Creasman,1993)** . Several investigators have provided well documented evidence that cystic , adenomatous and atypical hyperplasia if left untreated may ultimately progress to invasive cancer **(Gusberg,1947, and Kurman et al.,1985).**

Endometrial hyperplasia includes a varied group of histologic patterns characterized by overgrowth of glandular and stromal elements together with increased vascularity and lymphocytic infiltration, it may occur in any age group, but it is seen frequently at the two extremes of the reproductive period **(Kistner, 1990).**

Most endometrial hyperplasia is thought to result from persistent , prolonged unremitting estrogen stimulation of the endometrium **(Creasman,1991).**

In classifying hyperplasia , to date, no agreement about terminology has been reached. On histologic grounds according to the patterns of growth of endometrial glands, hyperplasia of the endometrium can be classified into three types ;cystic , adenomatous and atypical , more than one type may be present **(Tavassoli and Kraus, 1978, and Ramzy, 1990)** . In **1984,** the International Society of Gynecological pathologist presented a classification that primarily takes into account cytological abnormalities into three categories:

1- Simple hyperplasia .
2- Complex hyperplasia (adenomatous hyperplasia without atypia).
3- Atypical hyperplasia (adenomatous hyperplasia with atypia) **(Kurman , 1988) .**

Many methods can be used to evaluate those patients with endometrial hyperplasia, non invasive methods include ultrasound to determine endometrial thickness in asymptomatic postmenopausal women **(Sakamoto, 1984)** ,and invasive methods which include many techniques for sampling of the endometrium either for cytological analysis or histological examination. The ideal sampling method for cytological sampling must be acceptable to the patient, of low cost, simple and appropriate for outpatient investigation without the need for hospitalization or general anesthesia **(Creasman and Weed,1976, and Mencaglia et al., 1990).**

In general , endometrial cytological samples may be obtained by - washing - aspiration and brushing and in the field of endometrial

hyperplasia , cytology require special skills in its interpretation and cytologic evaluation of endometrial hyperplasia is difficult , although it provides excellent results in the hands of some investigators **(Kashimura et al.,1988).**

Chromosomal instability as an early feature of numerical aberrations are recognized as an early feature of malignant transformation and the total chromosomal content of tumor cells can be reflected by quantitative **DNA** analysis of tumor cells using **DNA** cytometry **(Iversen ,1986)** .

The measurement of **DNA** ploidy status and **S**- phase fraction **(SPF)** is likely to become a valuable adjunct to the clinical and histopathological assessment of malignant and premalignant lesions . Tumor ploidy reflects the biological behavior of a large number of tumor types; diploid tumor in particular have a relatively good prognosis **(Friedlander et al., 1984) .**

DNA aneuploidy, corresponding to numerical chromosomal aberrations turned to represent an internationally accepted marker for malignancy , and this means that the detection of cells with aneuploid sets of chromosomes is equivalent to the detection of neoplastically transformed cells . Aneuploidy is a well recognized feature of human tumors , but the investigation of its biological and clinical significance has been hampered by technological constraints **(Friedlander et al., 1984).**

Quantitative **DNA** analysis reflects the total chromosomal content of tumor cells and can now be determined rapidly and reliably using flow

cytometry (**FCM**); this has resulted in renewed interest in its potential clinical applications **(Wheeless, 1991).**

The discovery of oncogenes has led to an increased understanding of the biomolecular abnormalities associated with malignant transformation . In this regard , it has been shown that viral oncogenes are derived from cellular genes that normally participate in processes of cellular growth and differentiation **(Watson ,1986).**

In transforming retroviruses and human malignancies these genes are thought to have acquired the ability to elicit malignant transformation by various mechanisms involving either mutation or overexpression . Several of the retroviral oncogenes that have been sequenced have been shown to be homologous with peptide growth factors or their cell membrane receptors . For example , v-*sis* encodes one chain of platelet derived growth factor , whereas v-*erb B* is derived from the gene encoding the epidermal growth factor receptor **(Rubin et al., 1993) .**

In contrast to retroviral oncogenes , the ***c-erbB-2*** (also known as ***HER-2/neu*** or ***neu***) gene was first identified as the oncogene associated with the development of neuroblastomas in rats exposed to ethyl nitrosourea in utero **(Padhy et al., 1982)** . In this animal model it has been shown that ***c-erbB-2*** is oncogenic because of a single point mutation **(Bargmann et al., 1986 A).**

Evidence is increasing that proto-oncogenes and cancer suppressor genes are involved in the development and /or progression of gynecological malignancies . Overexpression of ***c-erbB-2*** has been

reported to occur in approximately 15% to 40% of breast , ovarian and endometrial cancers **(Slamon et al., 1987,and Slamon et al., 1989).**

While histopathological examination remains an indispensable tool of the surgical pathologist in the diagnosis and evaluation of patients with gynecological malignancies , the advancement to technology and the development of new knowledge regarding neoplastic transformation are providing basis for new opportunities to improve patients care **(Sasano and Garrett , 1992) .**