CYTOLOGIC SCREENING OF DYSPLASIA OF THE CERVIX IN EGYPTIAN FEMALES

THESIS

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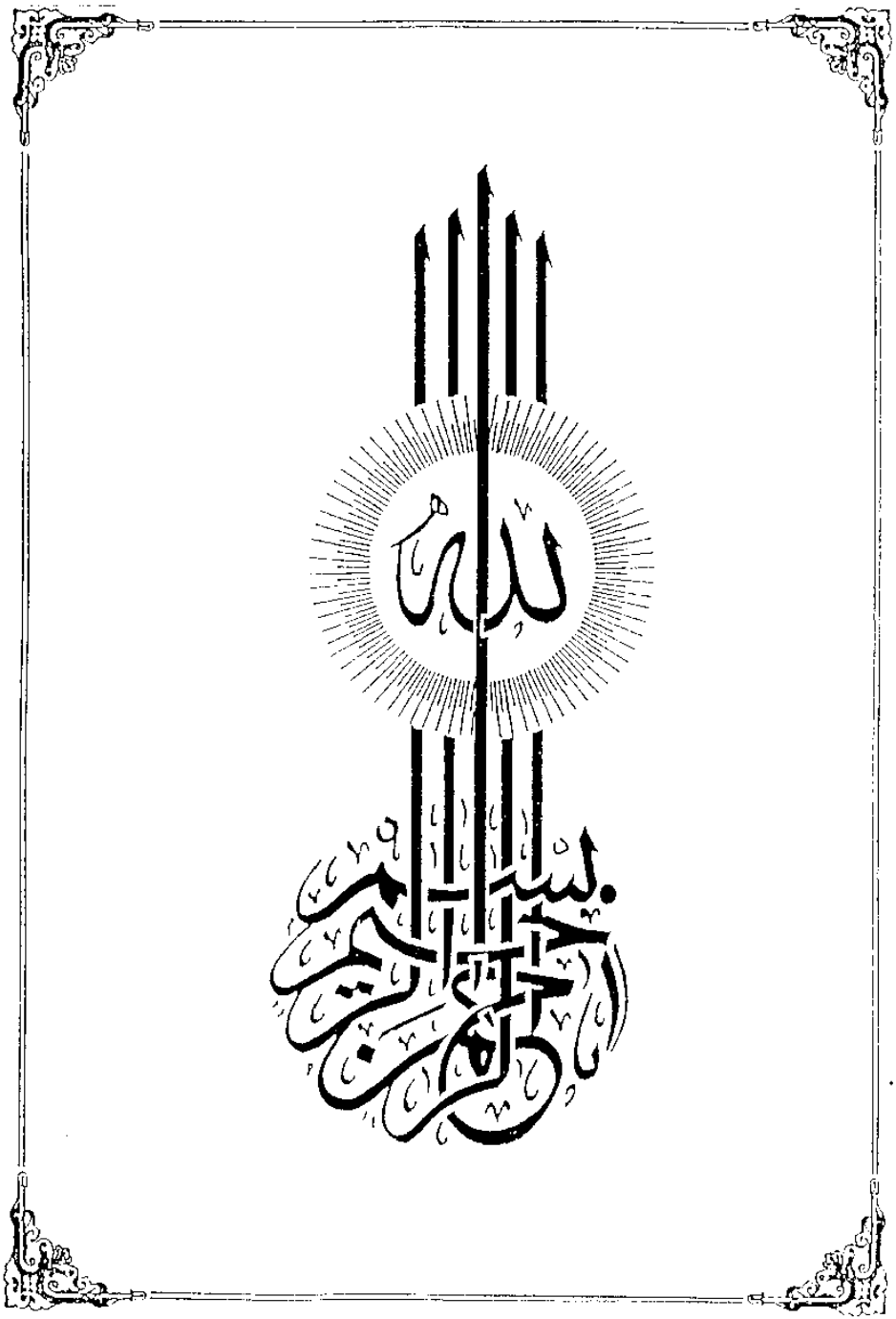

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INTRODUCTION AND AIM OF WORK

I N T R O D U C T I O N

Carcinoma of the cervix uteri is one of the most important diseases with which the gynaecologist most contend. This is true, not only because of the frequency with which the pre-invasive and invasive forms of the disease are encountered, but also because much is known about the natural history of the cancer cervix which may serve as a model for the early diagnosis and treatment of other cancers.

The unique accessibility of the uterine cervix to direct visual examination and the possibility of cellular and tissue sampling have permitted intensive investigations of pre-malignant lesions of the cervix.
Cervical cancer does not develop suddenly from normal tissue, but is preceeded by intraepithelial histopathological lesions.
When these lesions are recognized early and successfully treated, it is possible to decrease the frequency of cervical cancer.

Cytodiagnosis is relatively inexpensive, painless and more or less accurate in diagnosing cervical dysplasia and cancer. As such it is ideal for population screening

for the early detection of asymptomatic cervical neoplasia. Cytology remains the most practical and economical method for early detection of cervical cancer.

All women, regardless of age, should be screened regularly when they begin sexual activity.
Screening intervals depend on many factors, but are preferably done every year.
The likelihood of a woman having an abnormal "pap" smear after three subsequent negative smear is very low.

Basic concepts of pre-malignant lesions of cervix will be considered in this essay, also with special stress on the complementary role of diagnostic methods other than cytology.

Aim of the Work :

Early detection of carcinoma of the cervix and allied conditions in a sector of Egyptian females and to find out the incidence of cervical intra-epithelial neoplasia (CIN) changes among this group.

REVIEW
OF LITERATURE

ANATOMY AND HISTOLOGY OF THE CERVIX

- Gross Anatomy of the Cervix:

The term cervix (taken from the latin,meaning "neck") is the most inferior portion of the uterus protruding into the upper vagina. The vagina is fused circumferentially and obliquely around the cervix, dividing it into an upper, supravaginal and lower, vaginal portion.

The cervix measures in the adult nulligravida 2.5 to 3 Cm in length, and its normal position is slightly angulated downward and backward. The vaginal portion (portiovaginalis) of the cervix is centered by the external os , a circular (in the nulligravida) or slitlike (in the parous woman) opening. The external os is interconnected with the internal os by the cervical canal. The canal is an elliptical cavity, measuring in its greatest width 8 mm.
The blood supply of the cervix is provided by the descending branches of the uterine arteries, reaching the lateral walls along the upper margin of the para-cervical ligaments (cardinal ligaments of Mackenrodt). The venous drainage parallels the arterial system. The innervation of the cervix is chiefly limited to the endocervix and peripheral deep portion of the ectocervix. This distribution is responsible for the relative insensitivity to pain of the

portio vaginalis. The cervical nerves derive from the pelvic autonomic system, the superior, middle and inferior hypogastric plexuses (Ferenczy, 1982).[a]

- Embryology of the Cervix:

The cervix uteri is differentiated into two segments, namely, the portio or ectocervix that area covered by stratified squamous epithelium, and the endocervix lined by high columnar mucous secreting elements. The ectocervix is derived from the invading epithelium of the urogenital sinus , or possibly the vaginal plate epithelium of the united mesonephric ducts.

The endocervix is of paramesonephric origin. Embryologically there is definable secretory activities in the endocervical glands during late embryonic life.

Neoplastic variations demonstrate dramatically this embryologic differentials. Endocervical adenocarcinoma simulate that seen in the endometrium and ovaries, conversely the lesions arising at the squamocolumnar junction are lower genital canal neoplasms (Novak and Woodruff, 1979).

Histology of the Cervix:

Some histological terms:

1) Original Squamous Epithelium: is the squamous epithelium which is laid down at the time of organogenesis. Usually it covers the vagina and most of the ectocervix.

2) Original Columnar Epithelium: refers to columnar epithelium laid down at the time of organogenesis. It is usually confined to the endocervical canal but commonly covers part of the ectocervix.

3) Squamo Columnar Junction: is the line of demarcation between columnar and squamous epithelium.

4) Metaplasia: refers to the process by which columnar epithelium is replaced by squamous epithelium. It is stressed that this is a physiological process which occur to a greater or lesser degree in all women.

5) Transformation Zone: refers to that part of cervix which has been the site of metaplasia, it is recognisable both colposcopically and histologically (Jordan, 1985).

The cervix is made up of admixture of fibrous, muscular and elastic tissues of which the fibrous connective tissue is the predominant component. Smooth muscles, making about 15% of the substance, is mainly located in the endocervix. The portiovaginalis being virtually devoid of smooth muscles, by contrast, at the isthmus 50 - 60 % of the supportive tissue made of muscular elements arranged in concentric fashion, serving the function of a sphincter (Ferenczy, 1982)[a].

1) Columnar Epithelium:

The mucosa of the endocervical canal is composed of a single layer of mucus secreting columnar epithelium which lines the surface and underlying glandular structure.
The latter are traditionally called compound, tubular racemose endocervical glands.
Fluhman, however, using three-dimensional plastic reconstruction from serial histologic sections has demonstrated that the endocervical glands actually represent deep uncrossed cleft like infoldings of the surface epithelium with numerous blind, tunnel like collaterals (Fluhman,1961). Because of the complex organization of these clefts or grooves, including oblique, transverse, and longitudinal arrangements, in histological section they often appear as single glandular units. The epithelial lining of the cleft is identical with that lining the surface and consequently the endocervical mucus producing apparatus is not considered glandular, but a complexly infolding mucinous membrane , (Ferenczy, 1982).[a]

- Microscopically:

The columnar epithelial cells characteristically have basally placed nuclei and tall, uniform, finely granular cytoplasm filled with mucous droplets. These have great

affinity for alcain blue stain, reflecting their sulfated sialic acid mucopolysaccharide content (Fand, 1973).

- Electron Microscopically:

The columnar epithelium lining the endocervical canal and occasionally extends into the ectocervix. It is made of tall cylinder and elongated columnar cells uniformly arranged in one layer and closely packed in a "cobblestone" pattern. The nuclei are round or oval and generally situated in the lower third of the cells, although during active secretion, as in pregnancy or at ovulation peak at Mid-cycle, they are found in the middle or bases of the cells. The bases of the cells are attached to basement membrane by hemidesmosomes. The columnar cells are of two types, non ciliated secretory cells, and kinociliated cells (Hafez, 1983).

Secretory Cells:

They utilize both apocrine and merocrine methods of secretion. They have a dome shaped raised surface covered with many short microvilli 2 x 0.2 um wide. Secretory cells stain deeply with periodic acid schiff stain (PAS) and become engorged with heterogenous secretory granules . Fibrille bodies are frequently noted in their cytoplasm , a storage form of glycoprotein (Phillip, 1975).

Ciliated Cells :

The ciliated cells are covered with kinocilia which beat rhythmically towards the cervical canal and vagina. Ciliated cells are more frequent in the endocervical canal particularly at the cervicoendometrial junction but rarely on the ectocervical columnar epithelium.
They have oval or rounded nuclei with fine chromatin distribution. The cytoplasm is characterised by numerous mitochondria, free ribosomes, occasional lysosomes and profile of rough and smooth surface endoplasmic reticulum. The luminal surface exhibits atypical cilia similar to those in the endometrium and oviduct, they also have microvilli interspersed with kinocilia. Their function is not clear, although it is assumed that they are involved in the mucociliary clearance of the mucous from adjacent secretory cells (Hafez, 1983).

2) Squamous Epithelium:

The exposed or vaginal portion of the cervix is generally lined by a non-keratinizing squamous stratified epithelium which is reforced to as "the native portio epithelium". The native portio epithelium is remodeled by proliferation, maturation and desquamation during the reproductive period. The epithelium is completely replaced by a new