بسم الله الرحمن الرحيم

قالوا سبحانك لا عـــلم لنـــا إلا ما علمتنا

إنك أنت العليم الحـكيم

صدق الله العظيم

IN THE NAME OF ALLAH, THE BENEFICENT,
THE MERCIFUL

They Said : " Be glorified we have no knowledge except that which you have taught us Indeed you are the knower, the wise " .

HISTOPATHOLOGY OF RECURRENT CHRONIC INFECTION OF THE CERVIX AND ITS RELATION TO SPECIFIC AETIOLOGICAL FACTORS

THESIS

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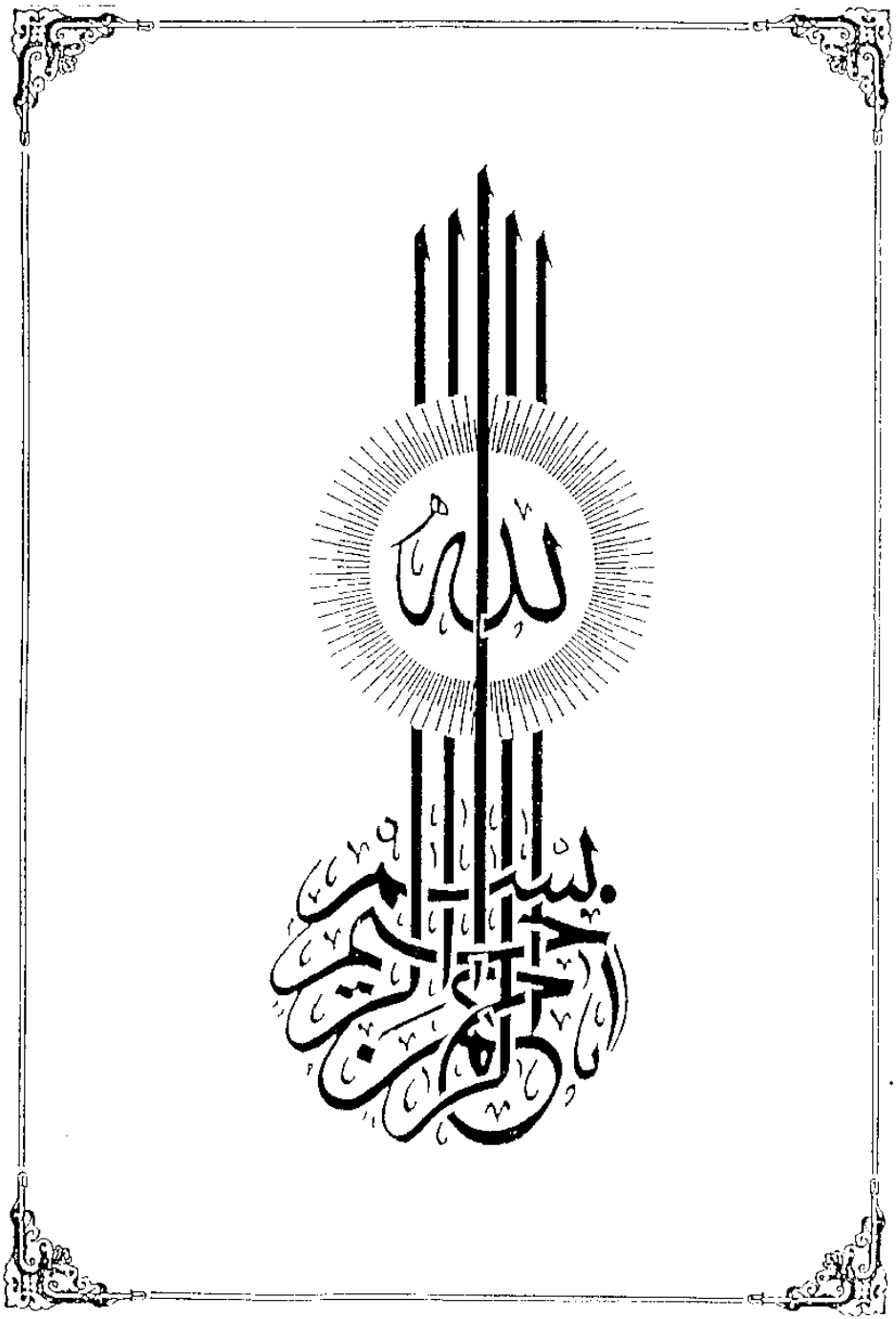

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INTRODUCTION

Chronic cervicitis is one of the commonest gynaecological disorders, and the symptoms it produces as vaginal discharge, low backache, congestive dysmenorrhoea, menorrhagia and dyspareunia contributed for most gynaecological complaints.

Personal, familial and community hygiene may act as contributing factors, with special emphasis on sexual hygiene, as the vast majority of patients are sexually active women. Still, the most important aetiological background is tissue trauma usually of repeated badly attended childbirths.

The recurrence of chronic cervicitis after the routine procedure of electrocautery or cryocautery, and even after repair of lacerations, directs our attention to other hidden aetiological factors, missed by the routine diagnostic aids. Such factors could be specific inflammatory diseases, granulomata, cervical intraepithelial neoplasia (CIN) or invasive cancer.

The proper evaluation of these factors is not well categeorized in relation to the condition of the unhealthy cervix.

AIM OF THE WORK

The objective of this work is to investigate the role of pyogenic bacteria, Trichomonas vaginalis, cervical intraepithelial neoplasia and invasive cervical carcinoma in the aetiology of chronic infection of the cervix and its recurrence.

Correlation of the cytopathic effect of the previously mentioned organisms, and others, incidentally found; with the different benign epithelial changes as well as with the pathogenesis of cervical intraepithelial neoplasia and invasive cancer, will be carried out.

The possible role - if any - of contraceptive methods used, in the aetiology of recurrence of chronic cervicitis will be studied, with special attention to their cytopathic effect, and any assumed role in the initiation or promotion of cellular atypia and other histopathological epithelial changes.

REVIEW OF LITERATURE

MICROBIOLOGY

I. Normal bacterial flora of the cervix during the child-bearing period:

Knowledge of the bacterial microorganisms which comprise the flora of the cervix uteri is important in understanding the aetiology of cervicitis. Other microbial and environmental factors are also involved in the process of infection. Their interaction with the flora must be considered.

Only through investigation of all the contributing factors, can we begin to elucidate the mechanism by which, some patients become infected and others do not, and also the mechanism by which, recurrence of infection occurs.

Aerobic gram positive cocci were isolated from 85% of cultures, and of these, staphylococcus epidermidis was the most common (Marilyn et al. 1975).

Fredreick (1955), Hanel (1958), Karsaky (1961) and Kotcher (1963), stated that staphylococcus aureus was not uncommonly recovered from cervical swabs. Kotcher (1963) pointed out that its association with cervicitis had not been documented. Harold Fox (1974), on the other hand reported the isolation of this organism from the endocervix in patients with chronic cervicitis.

Hinter (1958) detected haemolytic streptococci in 16.9% and non-haemolytic streptococci in 20.8% of the cervical swabs of healthy women.

Neisseria gonorrhoea was reported in 1% of healthy women. (Marilyn et al. 1975).

Diphtheroids which are gram positive bacilli have been isolated by Laughton (1950), Leppaluoto, P. (1974) and many other workers from vaginal and cervical swabs. They are usually non pathogenic, although, Holman and Mathieu (1960) reported them in a case of membranous cervicitis.

Hanel (1958) and Graham (1959), reported the frequent detection of E. coli from cervical swabs of healthy females. Marilyn et al. (1975), reported that 41 aerobic gram negative bacilli were isolated from 34 cultures among 100 cultures investigated, E. coli made up 68.3% of the aerobic gram negative bacilli isolated.

Leopold (1953), Gardner (1955) and Dukes and Gardner (1961), isolated Corynebacterium vaginale from vaginal and cervical swabs of healthy women. Ledger, W. J.(1977), stated that this organism is not a normal cervical inhabitant, and it is always related to a pathological process. Edmunds (1959) found this organism in 5% of normal cervical swabs, but

he believed that these organisms play an important role in puerperal sepsis.

Moore (1954) was able to isolate 10 strains of vibrios from cervical swabs and concluded that they were probably not responsible for cervicitis.

Anaerobic organisms have a great share of the normal microbial cervical flora.

Anaerobic streptococcus was isolated from the cervix in 40% of women by Soule and Brown (1932), 33% by Gorbach et al. (1973), and 74% by Marilyn et al. (1975).

Other anaerobic gram positive cocci, mainly anaerobic staphylococcus, were also isolated (Marilyn 1975).

Gorbach et al. (1973), reported isolation of Bacteroides species, which are anaerobic gram negative bacilli, in 57% of healthy women. Marilyn et al. (1975) isolated 32 isolates of anaerobic gram negative bacilli from 29% of women investigated. The majority were Bacteroides species. The principal varieties being Bacteroides melaninogenicus, B. fragilis and B. corrodens. Neary et al. (1977), assumed that the carrier rate varied with the stage of the menstrual cycle, being lower in the week or two before menstruation than after its onset.

Marilyn et al. (1975) isolated 41 strains of anaerobic gram positive rods, both spore-forming and non-spore forming from 38% of healthy women. Gorbach et al. (1973) put an incidence of 17% for Clostridia.

Veillonella, which are anaerobic gram negative cocci, were isolated from 15% of healthy women (Marilyn et al. 1975).

The recovery of certain anaerobic organisms,considered pathogenic, e.g., Bacteroides fragilis and Clostridium perfringens, from the cervices of healthy women demonstrates the need for careful interpretation of the results of cultures taken from the site of infection. As noted by Ledger and Hackett (1973) with Clostridium species, clinical symptoms must be considered in addition to culture results before diagnosing a Clostridial infection. This is true for determining the aetiologic agent of any infection from a site where a mixed flora is normally present.

Changes in cervical bacterial flora during pregnancy and puerperium:

The majority of cultures from the endocervix taken in the antepartum period showed potentially pathogenic aerobic and anaerobic bacteria, even though there was no clinical infection (Stanley 1975). Most apparent was the progressive decline from the first to the third trimester

in the isolation of E. coli and anaerobic organisms such as anaerobic staphylococcus, anaerobic streptococcus and Bacteroides fragilis (de Louvois 1975). There was a significant increase in the incidence of isolation of certain groups of bacteria like aerobic gram negative bacilli, Group B, beta-hemolytic streptococci, anaerobic gram positive cocci, anaerobic gram negative bacilli and anaerobic gram negative cocci when the results of the cultures obtained late in the third trimester were compared with those obtained on the third post partum day (de Louvois 1975), (Marvin, Edward and Joyce 1980).

The incidence of isolation of most bacterial species, six weeks post partum was found, nearly the same, as that of the first trimester of pregnancy, except for E. coli and Bacteroides which were isolated more frequently at the end of puerperium (de Louvois 1975).

In summary, many potentially pathogenic bacteria can be isolated from cultures of the endocervix throughout pregnancy and the puerperium. The most striking differences in flora occurred between the last six weeks of pregnancy and the third post partum day.

The finding that many pathogenic organisms were present on the third post partum day may improve our understanding of puerperal sepsis, regarding endogenous source of infection (Goplerud et al. 1976).

II. MICROBIAL AGENTS INCRIMINATED IN CHRONIC CERVICITIS.

A) BACTERIAL:

Chronic cervicitis of bacterial aetiology is very difficult to assess. We have not only to isolate the responsible organism and testing its pathogenicity, but also to exclude the presence of other organisms interacting with the responsible pathogen. This interaction might be responsible for recurrence of infection (Bartlett et al. 1978).

Non-specific bacterial chronic cervicitis is more frequent than that caused by specific bacteria (Harold Fox 1974). The cervix is usually badly lacerated, with exposure of the endocervical mucosa and loss of the normal defense mechanisms. The offending organisms, usually being a mixed flora of vaginal origin, particularly all pyogenic bacteria, especially staphylococcus aureus, Groups B and D streptococci, coliform bacilli, especially E. coli and anaerobic bacteria particularly Bacteroides fragilis, Clostridium perfringens and anaerobic streptococci. (Harold Fox 1974). The bacteria burrow deeply into partially obstructed glands and their surrounding stroma giving rise to a mucopurulent, alkaline, irritating and often malodourous discharge. (Charles A. White 1968).

Christensen K. 1974, in a study of the frequencies of streptococci of Groups A, B, C, D and G. in urethra