TO MY PARENTS,
WIFE, KESHNIE AND
SON, POOVERSAN MOODLEY
AN AETIOLOGICAL STUDY OF WHITE VULVAL SKIN LESIONS AMONGST PATIENTS ATTENDING THE GYNAECOLOGICAL CLINIC AT R. K. KHAN HOSPITAL, DURBAN

BY

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DECLARATION

I, Manivasan Moodley, hereby declare that the work on which this thesis is based is original, and that neither the whole work nor any part of it has been, is being, or is to be submitted to another University.

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ABSTRACT

BACKGROUND

White vulval skin lesions may be due to various conditions, including benign and non-benign causes. The dilemma faced by the clinician with such a patient is the aetiology of the lesion, as well as the approach to management.

AIM

To establish the aetiology of white vulval skin lesions in patients attending the gynaecology clinic and to evaluate the role of Collin's test and vulvoscopy.

SETTING

R. K. Khan Hospital, which is a secondary level hospital in Durban, KwaZulu Natal.

METHOD

Sixty-two patients with white vulval skin lesions whom consented to the study were recruited. The investigations consisted of Pap smear, colposcopy of the vulva [Vulvoscopy], perineum and where appropriate, vaginoscopy and colposcopy; Collin's test and biopsy of all abnormal areas detected by these tests.
RESULTS

Pruritus vulvae was the commonest presenting symptom [70%]. No vulvoscopy abnormalities were detected in 97% of patients, whilst 3% had acetowhite areas indicative of Human papilloma virus infection. Collin’s test was positive in 40% of patients, although, histologically these areas were benign. All patients in the study had benign lesions on histology.

CONCLUSION

All patients in this study had benign causes of white vulval skin lesions. However, this cannot lead us to conclude that there is no role for doing Vulvoscopy and Collin’s test, as premalignant and malignant lesions should be detected by these tests had they been present.
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1. **INTRODUCTION**

One of the commonest symptoms of vulval diseases is pruritus vulvae. [1] It has also been shown to be one of the commonest symptoms for which women attend a gynaecological clinic. [2,3,4,5] Another important symptom is that of vulval pain [Vulvodynia]. Vulvodynia is defined as chronic vulval discomfort, characterized by the patient’s complaint of burning, and sometimes stinging, irritation and rawness. [6] There are various clinical entities, which constitute the syndrome of vulvodynia [7] viz. vulval dermatoses, cyclic vulvitis, vulvovestibulitis syndrome, essential or dysaesthetic vulvodynia; vulval papillomatosis and miscellaneous causes such as neuroma of the vulva. [8]

There are many causes of pruritus vulvae. Examples include infections such as candidiasis, diabetes mellitus, hepatic or biliary disease, haematological conditions like polycythaemia, systemic dermatoses, amongst others. Although some authors [9] differentiate between pruritus and vulvodynia, the sensations of itching and pain respectively, are conducted by the unmyelinated type C nerve fibres. The stimuli for both these sensations however, are quite different. It is therefore important to examine these patients thoroughly to look for precipitating factors and to establish the cause. The patient with “Burning Vulva Syndrome” [10] seldom has gross abnormal physical findings. Dermatological manifestations of vulval disease
may be confusing, the cause may be ambiguous and the course of treatment usually long and frustrating. If the patient does not complain of a specific vulval symptom, the vulva is often overlooked during a routine gynaecological examination and is often simply "the means to go through" in order to perform the routine digital examination or pap smear.

A systematic approach to establish the aetiology of the patients' symptomatology is necessary. Various authors \[9,11,12,13,14\] have advocated an approach, which includes a thorough physical examination, pap smear, colposcopy of the vulva, vagina, cervix and perineum, Collin's test and biopsy of all abnormal areas detected by these tests. The role and need to do these tests have been questioned, since there are both false negatives and false positives associated with colposcopy \[15\] and Collin's test \[16\]. If a macroscopic lesion is present, the difficulty then, is to decide on which areas to biopsy in order to establish diagnosis.

Lesions found macroscopically and at colposcopy are classified according to the classification of Friedrich et al \[17\] [1983], in accordance with their appearance, white lesions, red lesions, dark lesions, ulcers, small tumours or large tumours. Many patients present with white vulval skin lesions, the cause of which varies from benign to malignant. Thus, in order to establish a correct diagnosis, a biopsy is necessary from the representative area. The
issue therefore is to decide on which area is the most representative. The limitations of the above mentioned investigations are noted and the emphasis of the study are the causes as well as evaluation of these investigations in-patients with white vulval skin lesions.

2. HISTORICAL PERSPECTIVES AND TERMINOLOGY OF WHITE VULVAL SKIN LESIONS

2.1 PREVIOUS TERMINOLOGY

The earliest description of a white vulval skin lesion was recorded by Weir [181 et al [1875]. He noted that these lesions were persistent, pruritic and benign. This case was presented among cases of leucoplakia of the tongue, a lesion recognized as premalignant. The issue of natural progression and especially the malignant potential of these lesions have been raised many times since, often, with an accompanying plea for a change in terminology. Schwimmer [192 et al [1877] used the term “leucoplakia”, which implied a potentially malignant change in mucosal and mucocutaneous tissue. The word “leucoplakia” is derived from leucos - white and placos - a flat plate. It was first used in medicine to denote a skin condition, which is characterized by a naked eye appearance of “white plaques” and was applied
originally to the tongue and mouth. This term was not intended to denote anything more than a clinical picture of white plaques, the plaques representing an increased deposition of keratin on the skin surface. Beneath this keratin various histological changes in the epidermis and dermis were described, with the possibility of there being two directly opposing features—namely, hypertrophy and atrophy.

Breisky et al [1885] introduced the term "Kraurosis" which means brittle. Yet, various authors later had different interpretations of this term. Taussig et al [1922] regarded the term Kraurosis as meaning "shrinkage", while Hunt et al [1940] regarded this term as meaning "white and dry". The British and American opinion on this term was also divided. The British view followed the teachings of Berkeley and Bonney et al [1909] as a condition affecting only the introitus, causing contracture and therefore dyspareunia, rather than pruritus. This concept was never accepted outside Great Britain. Taussig regarded contracture of the introitus merely as a result of excessive degenerative changes in the epidermis and dermis. The term Kraurosis is now recognized as lichen sclerosus.

Hallopeau et al [1889] described a condition of unknown aetiology in which there were small white patches of skin associated with atrophy of the vulval and perianal skin. This lesion was termed lichen sclerosus and has
survived all the changes in the literature over the past 100 years, in spite of the fact that there is neither lichen nor sclerosus present! “Lichen” implies thickening, yet the skin in this condition is thin and “Sclerosus” implies metabolic inactivity, yet several classic studies have proven that the tissue is indeed metabolically active, normal skin. Lichen sclerosus was also called lichen sclerosus et atrophicus. The terms “et atrophicus” is no longer used since it has been shown that the epithelium is metabolically active and not atrophic.

Taussig [21] et al [1922] introduced the term Leukoplakic vulvitis, a description of which was later recognized as mixed dystrophy [Lichen sclerosus with associated hyperplasia]. Taussig [21] et al [1922] further distinguished leukoplakic vulvitis from kraurosis not only on the basis of appearance and histology, but also on that of prognosis, stating that in his experience simple kraurosis had no malignant potential, while 50% of leukoplakic vulvitis progressed to malignancy. [21,27,28]

2.2 LATER CORRELATIONS

Wallace et al [29] [1951] and Wallace [30] [1955] in a series of accounts summarized by Wallace [31] [1971], attempted to overcome the confusion surrounding leukoplakia, kraurosis and leukoplakic vulvitis and their relation
to lichen sclerosus. They proposed that those cases clearly showing typical lichen sclerosus, clinically and histologically, should be noted as such. The terms Kraurosis and leukoplakic vulvitis should be dropped and where Kraurosis was seen without clear evidence of lichen sclerosus, this should be called "Primary Atrophy." Primary atrophy was regarded as having some potential for malignant change. Further, whereas Berkeley and Bonney [23] et al [1909] had found no hyalinization histologically, but much inflammation, the histology of primary atrophy was described by Wallace and Whimster [29] [1951] et al as an atrophic epidermis, reduced elastic tissue, hyalinised collagen and some inflammatory cells. They retained the term Leukoplakia as a histological entity, characterized by marked dermal hyalinization, sometimes a dermal infiltrate, a hyperkeratotic epidermis with lengthened, irregular forked rete pegs with or without cellular atypia.

Jeffcoate [32] et al [1961] tried to simplify the situation, beginning with an analysis of all putative causes of vulval malignancy. They reviewed the terms Leukoplakia and leukoplakic vulvitis and noted that in many situations the clinician expected the histopathologist to provide the diagnosis of leukoplakia and vice versa. They also noted that there were no clinical differences between leukoplakia, kraurosis and lichen sclerosus. They concluded that the same end point occurs due to different aetiological factors and that the vulval and perianal regions are subject to chronic skin changes, probably
conditioned by environment rather than causes. These skin changes irrespective of their appearances, for which a specific cause is unknown, are best given clinically by an all-embracing term such as “Chronic Epithelial Dystrophy.”

Gardner et al [33] [1969] suggested a histopathological classification with terms like Atrophic Dystrophy [Lichen Sclerosus], Hyperplastic Dystrophy and mixed Dystrophy [lichen sclerosus with foci of epithelial hyperplasia]. The sixth world congress of the International Federation Of Obstetricians and Gynaecologists was held in 1970, at which Gardner led a round table discussion of vulval diseases. From the efforts of those present, the International Society for The Study of Vulval Diseases [ISSVD] was formed. The purpose of this society included the classification, study and sharing of ideas and facts related to vulval diseases. It’s members included gynaecologists, pathologists and dermatologists.

Friedrich et al [33,34] [1976], reporting on behalf of the International Society for the Study of Vulvar Disease, recommended that lichen sclerosus et atrophicus, leukoplakia, neuro dermatitis, leukeratosis, Bowen’s disease, erythroplasia of Queyrat, Carcinoma simplex, leukoplakic vulvitis, hyperplastic vulvitis and kraurosis vulvae be deleted from the vocabulary of
vulvar diseases. Recommendations were made for an appropriate classification as follows:

i. Hyperplastic Dystrophy – with / without Atypia

ii. Lichen sclerosus

iii. Mixed Dystrophy – with / without Atypia.

Mixed dystrophy referred to lichen sclerosus with foci of epithelial hyperplasia. A uniform terminology to facilitate the collection and analysis of data on these diseases was thus developed. This classification is strictly histopathological, while the only clinical correlate is to note if the lesions were diffuse or localized, thick or thin, white or red.

2.2 THE CURRENT POSITION

Judging from the accounts of Berkeley and Bonney [23] et al [1909], the terms Kraurosis and Leukoplakic vulvitis are, essentially unitary and fully compatible with the different patterns of Lichen sclerosus. The same is true of the descriptions by Taussig [21] et al [1922] of these two terms. On reviewing the clinical and histological findings of primary atrophy, it was found that many patients with primary atrophy developed unequivocal lichen sclerosus. Therefore the use of the term primary atrophy has fallen away.
It was found that the entity "leukoplakia" corresponds to an active, painful fissured lesion of lichen sclerosus and is therefore regarded as a severe phase of lichen sclerosus. This term, presently, is reserved for use for oral lesions, at the recommendation of the World Health Organization and is defined as a white patch or plaque that cannot be characterized clinically or pathologically as any other disease. Thus, this term has been restored to its original oral domain and is no longer used to describe lesions on the vulva.

On reviewing the term "Dystrophy" it is noted that it comes from "dys" which means bad or difficult and "trophe" which relates to the nutrition or vascularity of the tissue. Yet, there are no proven nutritional or vascular aberrations present. It was also recognized that well-defined entities like psoriasis or eczema should have been recognized separately. The most problematic situation was when the term "atypia" was used as it frequently led many gynaecologists to radical vulval surgery or radiotherapy with its attendant problems in a condition of unknown malignant potential.

At the Ninth Congress of the International Society for the study of vulval diseases in 1987, changes were made in conjunction with the International Society of Gynaecological Pathologists, regarding terminology and classification. It was recommended that the terms "et atrophicus" be
dropped in patients with lichen sclerosus, as it has been shown that the epithelium is indeed metabolically active. The term Dystrophy has been replaced by the terms “Dermatoses” or “non-neoplastic epithelial vulval disorders” [NNEVD], emphasizing its non-neoplastic or benign nature. The term atypia is no longer used and where atypia is present, it is now grouped with the vulval intraepithelial neoplastic [VIN] lesions. The term hyperplastic dystrophy has been replaced by the term squamous cell hyperplasia. The term mixed dystrophy is no longer used as it has been recognized that lichen sclerosus may have a hyperplastic component without necessarily implying the presence of another disease entity.

Specific lesions or dermatoses affecting the vulva [e.g. psoriasis, lichen simplex chronicus, lichen planus, contact dermatitis, etc] would be specifically diagnosed and included under the term “other dermatoses”. The current classification of the vulval dermatoses is therefore:

i. Lichen Sclerosus

ii. Squamous Cell Hyperplasia

iii. Other Dermatoses
Examples of other dermatoses include:

i. Lichen simplex chronicus

ii. Lichen planus

iii. Psoriasis

iv. Contact dermatitis

2.3 CRITICISMS OF THE CURRENT TERMINOLOGY / CLASSIFICATION

There are two aspects of the current classification/terminology that are open to criticism. Firstly, as noted, the term lichen sclerosus does not appropriately describe the histological features. Yet, this term has survived all attempts to simplify the terminology. The second contentious issue is the term squamous cell hyperplasia, which was introduced to provide a descriptive term acceptable to both clinicians and pathologists. This term is not ideal, as epithelial hyperplasia may be the end result of a number of conditions. The diagnosis should be one of exclusion and should not be given as a pathological diagnosis if there is a definable dermatoses or pathological process which would explain the underlying process. There is also a possibility that clinicians and pathologists may confuse the term with
lichen simplex chronicus, which has squamous cell hyperplasia as one of its principle features.

3. CLASSIFICATION OF WHITE VULVAL SKIN LESIONS

Gross white appearance of vulval skin may be due to three general types of change:

i. Absence or loss of pigment

ii. Increased keratinisation [Hyperkeratosis]

iii. Relative avascularity

The following classification \(^{38}\) of white vulval skin lesions is recommended:

i. Depigmentation disorders – Leukoderma or Vitiligo

ii. Hyperkeratosis:

A. Chronic infections

B. Benign tumours

C. Vulval Dermatoses

1. Lichen sclerosus

2. Squamous cell hyperplasia

3. Other- Lichen simplex chronicus

   - Lichen planus

D. Vulval Intraepithelial neoplasia

E. Vulval Paget’s disease

F. Invasive vulval carcinoma
3.1 DEPIGMENTATION DISORDERS

Depigmentation can occur if the basal layer melanocytes are lost or destroyed or because of chemical malfunction, they are unable to synthesize melanin pigment. Vitiligo or leukoderma may be due to congenital or acquired absence of pigment. These terms are often used interchangeably. The congenital variety often appears at the menarche suggesting a relationship between pituitary gonadotropes and melanin stimulating hormone. Many parts of the body may be involved, although the anogenital area seems to be more common.

In the acquired type the melanocytes disappear from localized areas of skin. Trauma, infection and radiation scarring can cause depigmentation. In leukoderma, newly formed skin may not have acquired a melanocyte population, resulting in white skin appearance. In albinism there are normal melanocytes, which are prevented from forming melanin pigment because of an enzymatic defect.

3.2 HYPERKERATOSIS

A number of conditions are associated with excessive surface keratin layers. If keratin is wet, it becomes opaque and appears white in colour. The thicker the keratin, the whiter the skin appears. For this reason, hyperkeratotic
vulval skin, which is in an area of constant moisture, appears typically white in colour.

The end result of chronic infection may be scarring and thickening of the skin with white change. Benign tumours such as papillomatous or verrucous lesions may demonstrate areas of hyperkeratosis and white change. Skin can also appear pale when superficial blood vessels are constricted, when interposing distance between them and the surface is increased, or when they are numerically decreased by a sclerotic process. All three of these mechanisms are indeed active in the white skin lesions seen in the vulval dermatoses.

4. VULVAL DERMATOSES
4.1 CLINICAL FEATURES OF VULVAL DERMATOSES/NNEVD
4.1.1 LICHEN SCLEROSUS

Lichen sclerosus typically occurs in childhood, regress following the menarche and recurs after the menopause. The skin in affected areas appears white, crinkled, scaly and thin. [Photograph number 1, page 72] It usually affects the skin of the labia majora, minora, clitoris as well as perianal area with relative sparing of the area in-between. This produces the typical “figure of 8” appearance which is classical, but not pathognomonic of lichen
sclerosus. In untreated patients there is obliteration of the clitoris by oedema with phimosis and atrophy and shrinkage of the labia minora and introitus. This commonly produces the symptom of dyspareunia or painful coitus.

In the early stages of the disease, the labia minora may fuse with the labia majora and disappear completely as a result of atrophy. The skin may split in the midline especially between the clitoris and urethra. In the natural folds of the skin, fissures may develop. This may also occur in the posterior portion of the fourchette. The white plaques may become confluent and guttate; in which case it may resemble that of scleroderma, with which it is significantly associated. Both these conditions can become bullous, especially scleroderma resulting in confusion in making a diagnosis.

Up to 20% of patients with lichen sclerosus have extragenital lesions, which present as small ivory, shiny macules or papules, that become atrophic and are usually asymptomatic. Extragenital lesions may occur on any part of the trunk, upper and lower limbs. A common area is the anterior aspect of the wrists. The Koebner phenomenon often occurs. The Koebner phenomenon refers to the occurrence of lichen sclerosus at sites of trauma, when the lesion is also present elsewhere on the body. Lichen sclerosus has been noted to occur at the site of radiotherapy for carcinoma of the breasts.
in two patients who had no lesions elsewhere.\textsuperscript{[40]} The existence of oral lichen sclerosus is disputable and histological confirmation is rarely present.

Vesicles and bullae, sometimes haemorrhagic, may occur. Small telangiectases and purpuric lesions sometimes occur probably as a result of injury to the atrophic skin. The disorder is much less common in children than in adults. Published series show from 2\%\textsuperscript{[41]} to 15\%\textsuperscript{[42]} of cases begins before the age of 13. The earliest reported age of onset was 6 months.\textsuperscript{[43]} In Wallace's series \textsuperscript{[31]} [1971], 28 of 50 started between the ages of 3 and 6 years. The clinical features of childhood lichen sclerosus are the same as that in adults.\textsuperscript{[44]}

The general health remains normal and often the condition is asymptomic. A vaginal discharge may precede the vulval lesions in about 20\% of patients. However, the commonest presenting symptom is that of pruritus vulvae which may occur in up to 60-70\% of patients. It seems that the more hyperplastic the lesion, the more severe is the pruritic symptom.

**PROGNOSIS OF LICHEN SCLEROSUS**

Whilst it is generally agreed that extragenital lesions of lichen sclerosus usually remit following puberty, there is uncertainty as to the anogenital
lesions. Wallace et al [1971] noted that in two thirds of patients with anogenital lesions, the lesions cleared around the time of puberty. Detailed follow-up is usually not available. In Wallace's report, the regression is mainly of symptoms rather than signs. It seems therefore, that although the condition looks and feels better around the time of puberty, proof that it actually remits is lacking. The condition does not seem to remit in middle age, except in the extragenital sites. Therefore, it may very well be that lichen sclerosus does not remit at all. This is often supported by the fact that adult patients often recollect symptoms of lichen sclerosus in childhood. Adult women with lichen sclerosus may complain of dyspareunia, but pregnancy appears to be uneventful. [19]

4.1.2 Squamous Cell Hyperplasia

Squamous cell hyperplasia typically presents as thick white skin involving the labia majora, outer aspect of the labia minora, interlabial sulci and perineum. [Photograph number 2, page 73] In both lichen sclerosus and squamous cell hyperplasia there is hyperkeratosis producing the white skin appearance. In addition, in squamous cell hyperplasia, the rate of melanin production by the melanocytes cannot keep pace with the rate of growth of epithelial cells. Areas of squamous cell hyperplasia may be localized, elevated and well defined. In some patients the lesions are poorly defined. The vulva is usually
white in colour and due to the hyperplasia and hyperkeratosis, the skin is thick in texture.

In black patients the appearance may be dramatic and is often confused with vitiligo. However, in vitiligo the skin usually has a smooth surface. There may be fissures and excoriation, the result of chronic scratching. Many patients present with pruritus vulvae although some may present with soreness, burning and vulval pain [vulvodynia]. Most patients are younger than 50 years of age, although it may occur in the older patients. In a small percentage of patients, the lesions may be detected at routine gynaecological examination. There are an even smaller percentage of patients whose presenting complaint is one of a white vulval skin lesion.

4.1.3 OTHER DERMATOSES

4.1.3.1 LICHEN SIMPLEX CHRONICUS

Lichen simplex chronicus presents as thick, leathery white skin, which affects the labia. It is thought to be a secondary dermatoses, following chronic rubbing or scratching of the skin. Chronic contact or irritant reactions can provoke scratching as can any infection. The provoking stimulus may resolve, but lichen simplex chronicus persists because the patient continues to irritate the involved area. The affected skin becomes
lichenified, thickened and leathery with prominence of normal skin markings. [Figure 1, page 74] Pruritus is always a major symptom and with time, it may become impossible to tell whether the patients' scratching has triggered the itch or vice versa. Lichen simplex chronicus seems to develop more easily in-patients with atopic eczema. The lesions may be confined to the vulva or may be part of general dermatoses with the antecubital and popliteal fossae being the commonest extragenital sites involved. [45]

4.1.3.2 LICHEN PLANUS

Lichen planus is typically a pruritic eruption of shiny, smooth, flat-topped papules on the skin and white patches or erosions on the mucous membranes. [Figure 2, page 75] The papules are usually purplish-white in colour forming a lacy pattern. Patients first notice lesions on the lips and the gynaecologist may be the first to find asymptomatic vulval lesions. Almost two thirds of patients with lichen planus have mucous membrane involvement [391] and some have disease limited to either the genitailla or oral mucosae.

The lesions typically occur on the anterior aspect of the wrist, lumbar area of the back, medial thighs, ankles and shins. In the acute
widespread variety, lesions begin on the extremities and spread rapidly centrally to involve the trunk, sparing the face. Another type of lichen planus lesion is that described as the erosive lichen planus which may involve the vagina causing extensive desquamation of the vaginal mucosa, with resultant synechiae formation. A grey pseudomembrane is usually noted. The vestibule may be erythematous and friable with an adherent exudate. There may be marked resorption of the labia minora. Atrophy may occur including obliteration of the clitoral head. Patients sometimes complain of pruritus, burning, dysparenia and the feeling of "rawness". The onset of the erosive type of lichen planus may preceed or follows vulvovaginal lesions many months later.

4.2 HISTOPATHOLOGICAL FEATURES OF THE VULVAL DERMATOSES

4.2.1 LICHEN SCLEROSUS

The histological features of lichen sclerosus are usually typical. There is hyperkeratosis or thickening of the keratin layer producing the white skin lesions. The epidermis is markedly thinned with flat rete pegs. There is cytoplasmic vacuolization of basal cells and follicular plugging. Beneath the epidermis there is a characteristic zone of homogeneous, pink-staining, collagenous-appearing tissue which appears acellular. Oedema is usually noted in these areas. Immediately below this area, in the mid-dermal zone,
lies a band of chronic inflammatory cells made up mainly of plasma cells and lymphocytes. There may be areas of hyperplastic squamous epithelium present, which usually occurs secondary to chronic scratching of the vulval skin. [Photograph number 3, page 76]

4.2.2 SQUAMOUS CELL HYPERPLASIA

The histological features consist of a variable increase in thickness of the keratin layer [Hyperkeratosis] and irregular thickening of the malpigian layers [Acanthosis]. Acanthosis results in epithelial thickening associated with lengthening and distortion of the rete pegs into either clubbed or pointed structures. The granular layer is sometimes prominent. Due to the elongation of the rete pegs, the papillae become conspicuous and oedematous. A chronic inflammatory cell infiltrate consisting of plasma cells and lymphocytes is often present within the dermis. [Photograph number 4, page 77] Squamous cell hyperplasia is usually a diagnosis of exclusion when the acanthosis cannot be attributed to a specific dermatosis, or a pathological process that would explain the hyperplastic process. [46]

4.2.3 Lichen Simplex Chronicus

In well-developed cases of lichen simplex chronicus, there is hyperkeratosis, acanthosis, and elongation of the rete pegs, fibrosis of the papillary dermis
and a mild inflammatory infiltrate. [Photograph number 5, page 78] There
is also an underlying dermatosis seen which results in epithelial thickening.
[36]

4.2.4 LICHEN PLANUS

The histological features of lichen planus of the vulva are similar to that
found elsewhere in the body. These features include hyperkeratosis,
acanthosis, a dense subepithelial band-like infiltrate composed mainly of T-
Lymphocytes, which extends up to the basal layer where there may be
liquefaction, degeneration and the formation of colloid bodies. The rete pegs
are elongated and pointed. These histological features are as a rule, definite
and may be necessary if there are pale isolated papules similar to that of
lichen sclerosus.

4.3 AETIOLOGY OF VULVAL DERMATOSES

The aetiology of the vulval dermatoses remains obscure although various
theories have been suggested, viz.: 
4.3.1 LINK WITH AUTOIMMUNE DISEASES

An association of lichen sclerosus with autoimmune diseases has been suggested. Wallace\textsuperscript{[31]} et al [1971] suspected a significant association with vitiligo. Meyrick-Thomas\textsuperscript{[47]} et al [1983] studied the relationship between autoimmune diseases, autoantibodies and lichen sclerosus in 25 men. They found a significantly higher frequency of autoimmune related disorders compared to a control population. There was also a higher frequency of autoantibodies than expected in a normal male population.

Ridley et al \textsuperscript{[39]}, later confirmed these findings in a study of more than 200 patients. A later study by Meyrick-Thomas\textsuperscript{[48]} et al [1988] found autoimmune related disorders in 59.5\% of patients studied. Of the 350 women studied, 21.5\% had one or more autoimmune related disease, 21\% had one or more first degree relatives with autoimmune related disease, 42\% had an autoantibody titre greater than 1 in 20 and almost 60\% had one or more autoimmune related phenomenon, i.e. a personal or a family history of an autoimmune related disease including alopecia, vitiligo, thyrotoxicosis, hypothyroidism, pernicious anaemia, diabetes mellitus, systemic lupus erythematosus and primary biliary cirrhosis. The conditions most often linked in affected women are thyroid disease and alopecia.
Goolamali et al [1974] reported a link between patients with vitiligo and lichen sclerosus. In twenty-six patients with lichen sclerosus, it was found that 40% had anti-thyroid antibodies and 44% had antibodies against gastric parietal cell. It was therefore felt there could be a link between lichen sclerosus and an autoimmune process. It has been noted that there is a relationship between patients with Sjogren’s syndrome and vulval dermatoses. Thus, it is postulated that there may be a relationship between autoimmunity and vulval dermatoses.

Achlorhydria has been noted to be present in some cases of vulval dermatoses of which many were probably lichen sclerosus. Jeffcoate et al [1966] noted this to be the case in 23% of 269 patients with vulval dermatoses. Lavery et al [1984] found achlorhydria in 10 of 18 patients with “chronic vulval dystrophy” and speculated, about a relationship between the effect of urogastrone [epidermal growth factor] on the skin and on gastric acidity and the opposing effect of somastatin. Johansson et al [1986] noted immunoreactivity to a substance like vasoactive intestinal peptide in cells of the epidermis in two out of four patients with lichen sclerosus and cells of the epidermis to substance like vasoactive intestinal polypeptide.
In contrast, Harrington and Dunsmore\cite{53} et al [1981] noted a low occurrence of autoimmune phenomena and lichen sclerosus, especially with regards the natural history. This was further supported by the failure to demonstrate an association between lichen sclerosus and HLA-B 8 or DRw3, the tissue types found to have an increased prevalence in individuals with diseases considered to have autoimmune basis.

Meyrick-Thomas\cite{48} et al [1988] further noted no relationship between autoimmune phenomenon and the natural history of lichen sclerosus [sites of involvement, age of onset, onset in relation to menarche and menopause or the development of malignancy] of those with or without antibodies.

Harrington\cite{54} et al [1984] found a non-statistically significant increased incidence of HLA-B40 in 50 women with lichen sclerosus. Meyrick-Thomas\cite{55} et al [1984] also found a non-statistically significant association with HLA types in 92 women and 28 men with lichen sclerosus.

4.3.2 Hormone Dependency

It is well recognized that when lichen sclerosus occurs in pre-pubertal girls there is often resolution when puberty is reached. \cite{11} This would suggest that
Lichen sclerosus may be influenced by oestrogen, but the use of topical oestrogens have been disappointing. Cinberg et al [1945] noted an improvement in vulval lichen sclerosus following the application of topical testosterone and others have investigated this further. Friedrich and Kalra et al [1984] studied 30 patients with untreated lichen sclerosus and found reduced serum levels of dihydrotestosterone and androstenedione and significantly increased levels of free testosterone. When patients were treated there were significant increases in total testosterone and dihydrotestosterone levels than in a control group.

These findings provide the basis for the treatment of lichen sclerosus with testosterone cream. It is hoped that, by inundating the skin with substrate, some of it will undergo conversion, thereby exposing the tissues to the deficient hormone.

These authors suggested that there may be a block in converting testosterone to dihydrotestosterone and postulated a reduction in 5 alpha reductase activity. However, in females with documented reduction in 5 alpha reductase activity, there has not been shown to be any increase incidence of lichen sclerosus. Other authors have looked at hormone receptor levels and have found that there is elevated levels of progesterone receptors. This
could explain the beneficial effects of progesterone therapy for lichen sclerosus.

4.3.3 INFECTIVE LINK

There have been suggestions that lichen sclerosus may be due to a spirochetal infection. There is similarity in the skin lesions of scleroderma and Lyme disease. Lyme disease is caused by the spirochete Borrelia burgdorferi. There is similarity in the skin lesions of scleroderma and lichen sclerosus. However, these spirochetes as well as anti-Borrelia antibodies have not been found in lichen sclerosus. This link has not been confirmed. Karram et al [1988] studied the relationship between the vulval dystrophies and the presence of the human papilloma virus. There were no associations noted between the non-atypical dystrophies and the human papilloma virus.

4.3.4 MISCELLANEOUS CAUSES

There may be yet, other unknown causes, which may play a role in the vulval dermatoses. Barnes et al [1985] noted an increase in collagen inhibitor enzyme and an absence of collagenase in lichen sclerosus compared with the normal vulval tissue and that from other vulval conditions. The same authors later suggested that the activity of elastase is increased.
Bushbell [64] et al [1980] and Carli [65] et al [1991] suggested that the skin's immune system might play a role in the pathogenesis of lichen sclerosus. They observed an increase in activated T lymphocytes in the dermis as well as persistent increase in the number of epidermal Langerhan's cells in lichen sclerosus.


It is felt that although the environment of the vulva influences the various pathologic processes, the role of chronic trauma, allergy, nutritional deficiency, psychoneurosis, metabolic disturbances and other factors are unknown. There seems to be a likely relationship of chronic vulvovaginal infections like candidiasis to lichen simplex chronicus, especially in-patients with diabetes mellitus. [39]
The role of race or ethnicity is not clear, although, it appears to be commoner in Caucasian females. Barclay et al. [1966] and Dogliotti et al. [1974] described lichen sclerosus in Black patients.

4.4 RELATIONSHIP BETWEEN VULVAL DERMATOSES AND VULVAL MALIGNANCY

Lichen sclerosus at extragenital sites seems to have no risk of progression to malignant change. Basal cell carcinoma has been noted to occur in patients with lichen sclerosus. It is unclear if this association is fortuitous or not. Freidman et al. [1984] noted the association of malignant melanoma with lichen sclerosus on the vulva of a 14-year-old. One area of debate has been the risk of progression of the vulval dermatoses to invasive squamous cell carcinoma of the vulva.

McAdams et al. [1958] found lichen sclerosus to be present in 16 out of 400 cases [4%] and leukoplakia, presumably lichen sclerosus in 31 patients [12%], with vulval carcinoma. Buscema et al. [1980] studied 98 patients of squamous cell carcinoma and found “dystrophies” in 49 patients. Zaino et al. [1982] examined squamous cell carcinoma in 60 patients whom had vulvectomy. It was found that 32 patients had “Atypical Hyperplastic Dystrophy,” 15 lichen sclerosus, 14 hyperplastic dystrophy and
19 carcinoma in situ. Hewitt [77] et al [1976] found lichen sclerosus to be present in 96% of 104 women with squamous cell carcinoma.

Very few prospective studies have been done with regards to the risk of progression of the vulval dermatoses to invasive squamous cell carcinoma of the vulva. [22, 50, 72] It was noted that cancer rarely develops subsequently in women under close clinical supervision for chronic vulval diseases. Jeffcoate [50] et al [1976] noted that the risk of developing invasive carcinoma of the vulva in-patients with chronic vulval dystrophy in 138 women studied, ranged from 3-5% over a period of 3-25 years. Walkden [78] et al [1993] found the incidence of progression to be close to 9%.

Buckley [79] et al [1984] found that vulval intraepithelial neoplasia and lichen sclerosus may co-exist and this could increase the number of malignancies found with lichen sclerosus. Leibowitch [80] et al [1990] noted lichen sclerosus in 61% of women with vulval carcinoma. Fifty percent of these women had associated well-differentiated vulval intraepithelial neoplasia grade III. It was further observed that the undifferentiated form of vulval intraepithelial neoplasia grade III was not associated with lichen sclerosus. In those patients with carcinoma associated with lichen sclerosus, there was no evidence of the human papillomavirus [HPV/ DNA]. However, HPV/ DNA was found in association with severe vulval intraepithelial neoplasia.
In contrast, it was found that HPV type 16/18 was present in invasive squamous cell carcinoma in patients with lichen sclerosus.

In summary, the risk of vulval squamous carcinoma developing in a patient with vulval dermatoses is in the order of 1-5% over a prolonged period of time. The risk factors for the progression of the vulval dermatoses to invasive carcinoma include a history of lichen sclerosus in childhood, co-existence of HPV 16/18 and the erosive type of lichen planus. [39]

5. VULVAL INTRAEPITHELIAL NEOPLASIA [VIN]

5.1 EPIDEMIOLOGY OF VULVAL INTRAEPITHELIAL NEOPLASIA

During the past 20 years there has been an increase in the reported incidence of vulval intraepithelial neoplasia, especially in premenopausal, sexually active women. [81] Knight [82] et al [1973] reported 26 cases of carcinoma in situ of the vulva while Woodruff [83] et al [1943] reported on 44 cases diagnosed between 1966 and 1972. Sturgeon [84] et al [1992] noted that the incidence rate of VIN III had nearly doubled between 1973 and 1976 and 1985 to 1987. During the same period, however, the incidence rate for invasive carcinoma of the vulva remained stable. They also found that the incidence of VIN III increased from 1.1 to 2.1 cases per 100
In the past the mean age of presentation of VIN was 50 years. \cite{85} However, today the commonest age of presentation ranges between 28 – 35 years. \cite{81,86} This could be due to the fact that there is heightened awareness of neoplasia and increased tendency to take a biopsy as well as the frequent occurrence of viral infections of the lower genital tract.

There is no particular racial predisposition, with Whites and Blacks being equally affected. Whilst there is no relationship between the NNEVD and sexually transmitted diseases, there is a strong relationship between VIN and sexually transmitted diseases. \cite{81} The most common pathogens implicated include Human papillomavirus, Treponema pallidum, Trichomonas vaginalis, Gardnerella vaginalis etc. There is a common association with immunosuppressed states \cite{87,88} viz. renal transplants, systemic lupus erythematosus, cytotoxic agents etc.

5.2 **VIN AS A MULTICENTRIC DISEASE**

Vulval intraepithelial neoplasia is commonly associated with cervical intraepithelial neoplasia in 11 – 80\% \cite{89,94} of patients as well as with intraepithelial neoplasia of other genital tissues, including the anal canal. All
these intraepithelial neoplastic lesions are well-documented precursors of invasive squamous carcinoma in these areas. It is thought that a common oncogene affects the lower female genital tract, with the vulva and cervix being the most susceptible sites. When VIN is diagnosed, the chance of finding a concurrent cervical intraepithelial neoplastic lesion ranges from 11 – 80%.

5.3 NOMENCLATURE OF VIN LESIONS

In 1984 and again in 1987, the nomenclature committee of the International Society For The Study Of Vulva! Diseases\cite{39} proposed a classification for intraepithelial neoplasia involving the vulva. They grouped the diseases of squamous cell type under a single heading. On the other hand, Paget’s disease and melanoma in situ, having distinctly different histopathological appearances, histochemical characteristics and natural histories, were subclassified. The classification of VIN lesions depend on the level in the epithelium the dysplastic cells are found and is as follows;

A. Squamous:  
VIN – I [Dysplasia – mild]
VIN – II [Dysplasia – moderate]
VIN – III [Dysplasia – severe, carcinoma in situ]

B. Other: 
Paget’s disease [Intraepithelial]
Melanoma in situ [Level 1]
5.4 **CLINICAL FEATURES OF VULVAL INTRAEPITHELIAL NEOPLASIA**

Vulval intraepithelial neoplastic lesions commonly present as white skin lesions of the vulva, because of the hyperkeratosis. The lesions may be asymptomatic and discovered at routine gynaecological examination, or present more commonly as pruritus vulvae.\[^{90}\] The diagnosis is confirmed by histological examination.[Figure 3, page 79]

5.4 **HISTOPATHOLOGICAL FEATURES OF VULVAL INTRAEPITHELIAL NEOPLASIA**

The histological features of VIN are classified according to whether the cellular abnormalities and lack of stratification are limited to the lower third of the squamous epithelium [VIN I], middle third [VIN II] or upper third of the epithelium[VIN III].[Photograph number 6, page 80] In the basaloid form of VIN, a parakeratotic layer overlies an epithelium containing closely packed, non-stratified cells which show nuclear crowding and a high nucleocyttoplasmic ratio. In the Bowenoid form of VIN, there may be hyperkeratosis, premature cellular maturation, variable retention of stratification and pleomorphism and koilocytosis. Both the basaloid and the Bowenoid types may extend into the pilosebaceous units and sweat ducts. All these changes are confined to the squamous epithelium of the vulva.
5.5 COLPOSCOPIC FEATURES OF VIN

Andreasson\textsuperscript{[90]} et al [1985] and Buckley\textsuperscript{[79]} et al [1984] described the colposcopic findings of VIN lesions. These include abnormal vascular patterns with punctuations, mosaicism or vascular irregularities present in up to 60% of patients. The epithelial changes include the presence and degree of acetowhiteness of the epithelium following the application of 3% acetic acid. The colposcopic findings may be limited by the presence of thick keratin layers or congestion following infection or scratching.

5.6 PROGNOSIS OF VIN LESIONS

The risk of VIN grades I/II developing into invasive carcinoma is not clear, although, Friedrich\textsuperscript{[91]} et al [1981] regarded the risk to be low. It is generally felt that the behaviour of VIN III is not comparable to that of CIN III. Friedrich\textsuperscript{[91]} et al [1981] reported only 4 of 106 patients [4\%] with VIN III to have developed invasive disease. Andreasson\textsuperscript{[90]} et al [1985] quoted a figure of 2\% risk of progression of severe grade VIN. Most reported cases where VIN had progressed to invasive carcinoma have occurred where the patient was old or immunosuppressed.\textsuperscript{[87,88]}

Friedrich\textsuperscript{[91]} et al [1981] and Bernstein\textsuperscript{[92]} et al [1983] found that even untreated cases of aneuploid VIN III may undergo spontaneous regression.
Data on progression rates may be biased since majority of patients with VIN have been subjected to multiple treatments or diagnostic excisional biopsies. Bergeron et al [1987] noted that untreated long standing, histologically verified VIN has high progression rates in the order of 90 – 100%. Progression transit times range from 2 – 10 years. The human papillomavirus type 16 in association with VIN has been frequently noted to progress to invasive disease as compared to HPV types 6/11.

6. PAGET'S DISEASE OF THE VULVA

Extramammary Paget's disease is a slowly growing intraepithelial carcinoma containing vacuolated Paget's cells. Of significance is that Paget's disease may be associated with an underlying carcinoma of the apocrine structures of the vulva, e.g. Bartholin's gland as well as anorectal carcinoma, breast carcinoma and squamous cell carcinoma of the vulva, vagina and cervix. [94]

6.1 CLINICAL FEATURES OF PAGET'S DISEASE

Paget's disease of the vulva generally affects Caucasian women in the postmenopausal age group, with the mean age of diagnosis being 65 years. The clinical presentation may be striking, with white epithelium scattered over a bright red base.[Figure 4, page 81] As a rule, the disease begins on the hair-bearing parts of the vulva, genital folds or perianal region, but may
extend to involve the labia minora and introital structures. Less frequently, Paget’s cells may spread into the mucosa of the urethra, urinary bladder, ureters and even endocervix. The commonest presenting symptoms are pruritus vulvae, soreness and burning.

6.2 HISTOLOGICAL FEATURES OF PAGET’S DISEASE

The histological features of Paget’s disease are quite typical. The characteristic cell is the Paget cell which are large irregular cells containing clear vacuolated cytoplasm. The nuclei are vesicular and vary in size and shape. These cells may be isolated or occur in clusters at the tips or adjacent to the rete pegs deep in the epithelium. Paget’s cells can be found in the epidermis well beyond grossly visible normal surgical margins. Histochemical staining confirms the diagnosis of Paget’s disease and exclude melanoma or squamous cell carcinoma in situ.

7. INVASIVE CARCINOMA OF THE VULVA

Vulval carcinoma is rare, representing only 3–5% of genital cancers. Green et al [1978] found there is an increase in incidence to about 8% in recent years. Vulval cancer is mainly a disease of the aged, with the average age being the seventh decade. However, it has been documented in girls in their teens as well as in women in their 20’s and 30’s. No definite cause has been identified with regards the aetiology of vulval cancers. However, certain
risk factors have been identified such as a long standing history of VIN, viral agents such as human papillomavirus types 16/18, vulval condylomata and immunodeficiency states. [98, 99]

7.1 **CLINICAL FEATURES OF INVASIVE CARCINOMA OF THE VULVA**

Up to 75% of patients may present with a mass lesion of the vulva.[Figure 5, page 83] Between 27 – 71% of patients complain of pruritus vulvae and 6 – 41% have a discharge or present with bleeding. Some patients may also complain of pain. Whilst the macroscopic features may be exophytic or ulcerated, some patients may present with a white vulval skin lesion. [19]

7.2 **HISTOLOGICAL FEATURES OF INVASIVE VULVAL CARCINOMA**

There are many variants of squamous carcinoma of the vulva. Well-differentiated tumours usually have islands, anastomosing masses and infiltrating cords of squamous cells. These cells show progressive nuclear and cytoplasmic maturation and keratinization towards the center of these masses. The underlying tissue usually has plasma cells and lymphocytes in varying amounts.[Photograph number 8, page 84]
CHAPTER TWO

1. MANAGEMENT OF WHITE VULVAL SKIN LESIONS

1.1 INVESTIGATIONS

There have been various modalities of therapy proposed for the treatment of white vulval skin lesions. These include medical and surgical approaches. An area of uncertainty has been the approach to management of a patient with a white vulval skin lesion. There has been a tendency to treat these patients without any investigations. However, since the causes of a white vulval skin lesion are variable ranging from benign to malignant causes, many authors [11,12,13,14] advocate an approach which includes doing a Pap smear, colposcopy of the vulva [vulvoscopy], vagina and cervix, Collin’s test [toludine blue test] and biopsy of abnormal areas to establish the cause. This would guide clinical management as well as exclude the presence of underlying premalignant or malignant conditions.

1.1.1 ROLE OF COLPOSCOPY OF THE VULVA AND ADJACENT SITES

1.1.1.1 BACKGROUND

The colposcope [Photograph number 9, page 85] was introduced to evaluate abnormal cervical cytology since it has been shown to be reliable in predicting histological alterations. [100] Several studies [101,102,103] assessing various therapeutic agents in the treatment of the vulval dermatoses have used vulvoscopy in their methods. Vulvoscopy
is also used now to evaluate vulval complaints and pathology, for diagnostic workup in women with abnormal pap smears and to remove all vulvoscopically visible VIN III lesions. The main aim is to select abnormal sites to biopsy in order to exclude malignancy. The predictive value of vulvoscopy has been regarded to be uncertain mainly because normal vulvoscopy findings had not been determined in women without vulval complaints. It was therefore difficult to distinguish normal from abnormal findings.

1.1.1.2 NORMAL VULVOSCOPIC FINDINGS

Recently Van Beurden et al [1997] and Apgar et al [1996] have described normal vulvoscopy findings. It has been shown that vestibular erythema, vestibular papillomatosis and acetowhite lesions [30%] are common in healthy sexually active women without vulval complaints. It is thought that vestibular papillomatosis is probably congenital in origin and could be accentuated by any inflammatory condition. These micropapillae have been found to lack HPV DNA on hybridization studies.

A “cobblestone” appearance at the inferior part of the vestibule is thought to represent sebaceous hyperplasia, which occurs secondary to age or inflammation, producing hypertrophy of these glands. Non-specific acetowhite areas have been described at the junction of the
inferior part of the vestibule with the perineum. These changes are not due to the human papillomavirus infection but are thought to occur secondary to the trauma of intercourse, yeast infections or any other inflammatory conditions of the vulva. This type of acetowhitenening is usually diffuse and flat, whereas that due to HPV infection is slightly raised with satellite lesions. Acetowhite lesions without vascular abnormalities are common on the vulva. Therefore not every acetowhite area contains dysplastic cells.

1.1.1.3 LIMITATIONS OF VULVOSCOPY

There are 3 limitations to colposcopy of the vulva and perineum. These include hyperkeratosis preventing underlying vascular and epithelial abnormalities being visible, light reflection from keratin and the presence of hair – bearing skin at the site of the lesion. To overcome these problems, it has been recommended that hair be clipped at the site of the lesion and KY Jelly be applied on the skin to reduce the light reflection from the keratin. [111] KY Jelly is a non-toxic water-soluble agent, which does not interfere with other substances used during colposcopic examination.
1.1.1.4 **TECHNIQUE OF VULVOSCOPY**

Colposcopy is done using the technique described by Hatch et al [1993]. A colposcope with multiple magnification settings is necessary to facilitate the examination. The patient is placed in the lithotomy or dorsal position. The tissue to be examined is cleaned with saline, and then 3% acetic acid is applied. After 2 – 3 minutes the skin is examined under the colposcope for epithelial and vascular abnormalities. All abnormal areas are biopsied.

1.1.2 **COLLIN’S TEST [ TOLUDINE BLUE TEST]**

1.1.2.1 **BACKGROUND**

The Collin’s test was first used by Richart et al [1963] and later modified by Collin’s [1966], for vulval conditions as a diagnostic aid to delineate suspicious skin for biopsy. Toludine blue is a nuclear stain and when applied to tissues in vivo, becomes fixed to cell nuclei. Dilute acetic acid decolourizes any dye, which is not bound to nuclear material. In normal skin, keratin has no nuclei and therefore the dye is usually washed away with acetic acid.

Whenever there is a break in continuity of the epidermis, as occurs with an ulcer, or if nucleated squames are present in the upper epithelial layers, the skin would retain the dye. This would occur if
there are premalignant or malignant cells with nuclear material present in the upper epidermis.

1.1.2.2 LIMITATIONS OF COLLIN'S TEST

Reid [111] et al [1995] and Cavanagh [161] et al [1985] considered this test to be useful although, limited by false negatives associated with hyperkeratosis and false positives due to excoriation. Thus, areas, which are ulcerated or excoriated, as is often the case in patients with pruritus vulvae, would stain positive.

Freidrich [177] et al [1983] disregarded the false positive results and felt that much of the disappointment expressed with regards this test stemmed from the lack of understanding of its basic method of action. Many clinicians regard this test as a test for cancer, when in fact it is a simple test to indicate the presence of superficial nuclei. The presence or absence of cancer can only be confirmed by biopsy and histological assessment.

1.1.2.3 TECHNIQUE OF COLLIN'S TEST

The skin to be examined is first cleaned with saline or acetic acid. Toludine blue aqueous solution [1%] is then applied to the skin with a cotton swab and allowed to dry for one minute. The entire vulva is
then rinsed gently with 1-% aqueous acetic acid solution. Abnormal epithelium, if present, will stain royal blue.

The main argument for these investigations is to obtain directed biopsies rather than doing random biopsies,\textsuperscript{[14,114]} which could miss representative areas. This needs to be appreciated, as the abnormal areas can be quite large, making it difficult to select sites for biopsy. Another significant fact is that some of the lesions tend to be multicentric, therefore, colposcopy of these areas is necessary to determine the extent of the underlying disease process.

1.1.3 VULVAL BIOPSY

All abnormal areas detected by colposcopy and Collin's test need to be biopsied for diagnosis and treatment. Vulval biopsy is a minor procedure which does not require general anaesthetic and can be done as an out-patient procedure. Anaesthesia can be accomplished by the local infiltration of 1% lignocaine injected subcutaneously using a dental syringe. Biopsies can be taken using a special vulval skin biopsy instrument such as a Keyes biopsy punch [Figure 6, page 86] or cervical biopsy instrument or using a scalpel blade. The Keyes cutaneous instrument\textsuperscript{[17]} is used to core out a small circular plug of skin. It is obtainable in diameters ranging from 2 - 12 millimeters. The instrument is pressed against the skin, turned clockwise and
then anti-clockwise. A core of tissue is obtained containing epidermis and dermis. Alternatively, biopsy specimens can be obtained using a scalpel with a number 11 blade. An elliptical incision is made and the tissue removed. Minor bleeding can be stopped using a silver nitrate stick or a drop of Monsel’s solution. Large defects or significant bleeding is treated by inserting 3 – 0 chromic sutures. These biopsy sites usually heal within 2-3 weeks. Post biopsy discomfort is usually minimal and simple analgesia usually suffice. Specimens are sent in formalin solution to the laboratory for histopathological assessment.

2. THERAPEUTIC STRATEGIES: WHITE VULVAL SKIN LESIONS

Depending on the aetiology, there have various modalities of treatment proposed for the management of white vulval skin lesions. These modalities of treatment usually range from medical to surgical.

2.1 VULVAL DERMATOSES

Generally, a search should be made for any possible aggravating factors such as Trichomoniasis, Candidiasis and allergy to various agents. If any of these are present the patient should be treated appropriately.
2.1.1 LICHEN SCLEROSUS

Since lichen scierosus has atrophic histological features, treatment has generally consisted of using androgenic steroids such as topical Testosterone preparations. \[106\] Androgenic steroids are trophic hormones and are therefore appropriate in these conditions.

2.1.1.1 CHILDHOOD LICHEN SCLEROSUS

Lichen sclerosus in childhood, which is usually asymptomatic usually, does not require any treatment, except patient reassurance and follow up. The aim of treating childhood lichen sclerosus is to relieve the pruritus. The recommended initial treatment consists of topical 1% Hydrocortisone cream, alternating with bland emollient cream. \[43\] If there is no response to topical 1% hydrocortisone cream, then Progesterone ointment [compounded as 100 mg of progesterone in 1 ounce of petroleum] may be effective. Topical testosterone should not be prescribed for prepubertal females because of the risk of masculinising side effects. \[45\] Most children who respond to topical methods remain asymptomatic, although, careful follow up is necessary to exclude the development of malignancy in later life.
2.1.1.2 **ADULT LICHEN SCLEROSUS**

Various steroid preparations have been used for the treatment of adult lichen sclerosus. Initially 1% topical hydrocortisone cream should be applied. In most cases this is all that may be needed for the relief of pruritic symptoms. Testosterone propionate in sesame oil, 100 mg/ml is mixed in petroleum base to obtain a 2% ointment. This medication is applied 2-3 times daily for 3-6 months or until the pruritus has subsided. Therefore the frequency can be reduced over 1 to 2 years when it may be used once or twice weekly. Generally, testosterone and progesterone preparations for this purpose is not available commercially and has to be compounded by the pharmacist on request. Mahmud et al [1992] reported symptomatic improvement and reduction in lesion size in 80% of patients with lichen sclerosus treated with testosterone and corticosteroids.

One of the most effective agents reported for the treatment of vulval lichen sclerosus is clobetasol propionate [0.05%] [DERMOVATE, Glaxo, UK.] Bracco et al [1993] in a randomized comparative study compared the efficacy of topical testosterone, topical 2% progesterone in petroleum base, topical 0.05% Clobetasol propionate and a placebo. The symptoms, gross appearance and
histology were scored and repeated after 3 months of treatment. Only the clobetasol group improved significantly with regards relief of symptoms and improvement of objective and histopathological findings. Patients treated with clobetasol experienced no adverse effects, which can occur with 2% topical testosterone preparation. Clobetasol [0.05%] should be applied twice daily for one month, once daily for two months and then twice weekly for an additional 3 months. Equally satisfactory results were reported by Dalziel [118] et al [1991].

Bornstein [106] et al [1998] reported the results of topical testosterone [2%], clobetasol dipropionate [0.05%] versus topical testosterone propionate [2%] for the treatment of severe lichen sclerosus and confirmed a 75% resolution of symptoms with the clobetasol group. However, unlike the high success rates previously reported over the past 40 years with the use of testosterone, this study found a lower success rate of 20% in patients treated with testosterone.

Occasionally vulval pruritus is so severe that it is not relieved by topical drugs. Here, the subcutaneous injection of Triamcinolone acetonide [0.1%] 5 mg is diluted in 2 ml of saline and injected
subcutaneously. Satisfactory results have been recently reported with the use of oral retinoids for vulval lichen sclerosus. Bousema et al [1994] studied the efficacy of Acitretin [20 – 30 mg/day] for 16 weeks in a randomized, double-blind, placebo controlled trial using 78 patients. They found a 64% response rate in the acitretin group compared to 25% in the placebo group. The major drawback with the use of retinoids are their teratogenic potential and side effects. Young patients need effective contraception during therapy as well as for up to 2 years following discontinuation of therapy, as it has been shown that the drug can be stored in adipose tissue for up to 2 years after discontinuation of therapy, due to its highly lipophilic nature. Major side effects reported with these drugs include skin dryness, eye irritation, alopecia, myalgia and pseudoporphyria.

Sonnendecker et al [1993] and Larsen et al [1993] reported on the use of intralesional injection of interferon alpha 2b, when vulval dystrophy occurs in association with human papillomavirus infection. They noted the relief of chronic vulval discomfort and limited reversal of histological changes.
The role of surgery in the treatment of vulval lichen sclerosus is limited, as it has been shown that the risk of progression to cancer is very small. Also, lesions often reappear in transposed skin over the excised areas. Surgery is justified only if pre-malignant or malignant lesions are found in association with the vulval dermatoses.

2.1.2 TREATMENT OF SQUAMOUS CELL HYPERPLASIA

Hyperplastic lesions are best treated with topical corticosteroids. Various agents are recommended including 1% or 2.5% hydrocortisone cream, 0.025% Flucinolone acetonide, and 0.01% triamcinolone acetonide. There is a risk of atrophy of the tissues by using potent topical steroids. Therefore, once the pruritus has settled, the potent topical steroids should be discontinued and replaced with mild topical hydrocortisone cream.

Various adjuvant agents have been used with topical steroids for the relief of pruritus. Some of these agents include topical Crotamiton and Calamine lotion as well as oral anti-histamines such as chlorpheniramine 4 mg given at bedtime. For patients with recalcitrant pruritus, local injection of absolute alcohol subcutaneously has been described to relief symptoms for up to 12 months.
2.1.3 LICHEN PLANUS

Unfortunately, the course of vulval lichen planus is prolonged with or without treatment. Corticosteroids, systemic and topical, are recommended. Also, intravaginal Betamethasone valerate is recommended for vaginal lichen planus. If there is extensive desquamative vulvovaginal lichen planus, a short course of oral prednisone, up to 70 mg / day for 14 days may provide relief.

2.1.4 LICHEN SIMPLEX CHRONICUS

Lichen simplex chronicus responds to topical steroids. It is recommended that initial therapy should consist of potent steroids such as flucinolone acetonide used for 6 weeks to control the inflammatory response. Thereafter, lower potency steroids like triamcinolone acetonide 0.1% should be applied daily or twice daily for up to 2 months as response occurs. Topical 1% hydrocortisone cream should be used as maintenance therapy.\textsuperscript{[39]} In children mild topical steroids are recommended.

2.2 MANAGEMENT OF VULVAL INTRAEPITHELIAL NEOPLASIA

Since the early 1960’s and 1970’s, there has been a radical change in the management of vulval intraepithelial neoplastic lesions. The treatment has become more conservative with the recognition that spontaneous regression occurs, as well as the fact that progression to invasive disease may be less
likely in younger females. In addition, there may be functional impairment, cosmetic as well as psychosexual sequelae with more radical procedures.

Generally, treatment should be individualized according to the location, severity and extent of lesions. The presence or absence of factors increasing the risk of occult invasive carcinoma should be considered. Treatment modalities range from medical to surgical methods. Medical treatment includes topical 5% 5-Fluorouracil cream, photodynamic therapy using dihaematoproporphyrin and dinitrochlorobenzene sensitization therapy. The problems encountered with medical therapies include extensive tissue sloughing, severe discomfort, delayed healing, variable response rates and insufficient patient numbers to evaluate success.

Surgical therapy includes wide local excision, skinning vulvectomy, carbon dioxide laser therapy and cryotherapy. Skinning vulvectomy is reserved for very extensive four quadrant lesions followed by the application of split thickness skin grafts. Wide local excision is recommended for localised lesions provided a 1 centimetre clear margin of normal skin is excised. Excellent therapeutic and cosmetic results may be obtained with the carbon dioxide laser treatment of hairy and non- - hairy skin to a depth of 2 millimetres and 1 millimetre, respectively. Deeper vaporization would
destroy subcutaneous fat, skin appendages, resulting in delayed and painful healing, scarring, dyspareunia and alopecia.

Cryotherapy has not gained popularity mainly because it produces delayed and painful healing and failures or recurrences are common. \[122, 81\]

Generally the recurrence rates for the surgical methods are variable, ranging from 10%, if the surgical margins are free of disease, to 50% if the surgical margins have residual disease. \[124\]

2.3 MANAGEMENT OF PAGET'S DISEASE

There is a high incidence of associated carcinoma of the breast and genitalia in a patient with Paget's disease of the vulva. Therefore a thorough search for these tumours should be made as the treatment of these tumours takes precedence over the treatment of vulval Paget’s disease. If no associated malignancies are found, then the recommended treatment of the lesion consists of excision of the lesion down to subcutaneous fat, in order to exclude underlying sweat gland carcinoma. Previously, excision of the lesion with wide margins was recommended. \[39\] However, it has been found that recurrence rates of 12% occurs irrespective of the extent of histological involvement. \[91\]
2.4 MANAGEMENT OF SQUAMOUS CELL CARCINOMA OF THE VULVA

It is recognized that early invasive squamous carcinoma of the vulva can present as a white vulval skin lesion. If invasive disease is diagnosed then the current surgical staging should be used. Management should be individualized according to the stage of the disease and the trend is to use less radical surgery due to recurrence rates, psychosexual sequelae, complications and the fact that invasive carcinoma is now being diagnosed earlier in younger patients with smaller lesions. The surgical management consists of two main aspects. Firstly, surgery of the vulval primary lesion itself and secondly, management of the regional lymph nodes, where applicable, as described by Helm et al [1992].
CHAPTER 3: THE STUDY - AN AETIOLOGICAL STUDY OF WHITE VULVAL SKIN LESIONS AMONGST PATIENTS ATTENDING THE GYNAECOLOGICAL CLINIC AT RK KHAN HOSPITAL, DURBAN.

1. INTRODUCTION AND AIM OF THE STUDY

White skin lesions may be confined to the vulva or may involve the vulva as well as other parts of the body. These lesions may occur in all age groups but some tend to occur in childhood, regress following the menarche and recur after the menopause. The aetiology of white vulval skin lesions are classified into benign and non–benign causes. Whilst it is recognized that benign causes such as those which constitute the entity of vulval dermatoses [Lichen sclerosus, squamous cell hyperplasia and other dermatoses] commonly manifest as white vulval skin lesions, vulval intraepithelial neoplasia, Paget’s disease of the vulva and early invasive squamous carcinoma of the vulva can also present as similar clinical entities.

The dilemma faced by the clinician who manages a patient with a white vulval skin lesion is the exact cause in that particular patient. There is often uncertainty as to whether one should observe the lesion, biopsy the lesion or treat without biopsing the lesion. There is also a problem of knowing which site to biopsy since these lesions tend to be uniformly white and diffuse.
In contrast, some authors recommend a structured approach consisting of doing a Pap smear, colposcopy of the vulva, vagina and cervix and adjacent sites, where appropriate, Collin’s test and a biopsy of all abnormal areas detected by these tests. This may seem to be unnecessary to those who believe that many such lesions are benign, and justify treatment without workup or tissue diagnosis.

However, judging from the literature, it is evident that benign as well as premalignant and malignant conditions can present as white vulval skin lesions. It is also recognized that benign disorders such as the vulval dermatoses can present adjacent to premalignant and malignant lesions. It seems therefore that it is difficult to guess from just inspecting the lesion, as to whether the lesion is benign or not.

The modalities of treatment of these various conditions vary widely from medical to surgical methods. It would therefore be inappropriate to treat without biopsy or to biopsy the lesion randomly as there is a risk of not obtaining the representative areas that can be achieved by doing vulvoscopy or Collin’s test. The aim of the study was therefore, firstly, to determine the aetiology of white vulval skin lesions amongst patients attending the gynaecological clinic at RK KHAN Hospital and secondly, to evaluate the role of vulvoscopy and Collin’s test.
2. **PATIENTS AND METHODS**

Ethical institutional permission was obtained and all patients gave informed consent. The study was done over an 18-month period from January 1997 to June 1998. All patients with white vulval skin lesions as well as those patients with similar lesions in other parts of the body were recruited for the study. Initially an appropriate history was taken including complaints, age and parity. A thorough general examination was done to exclude similar lesions elsewhere in the body. The vulva was inspected and the distribution of the white skin lesion recorded. If there was no vulvovaginal infection, vulvoscopy was done using the method described by Hatch et al [1993]

Any abnormality detected by was noted and later biopsied as described below. A Collin's test was then performed using 1% toludine blue, which was applied to the vulval skin and washed off after 1 minute with 1% acetic acid. Those areas, which retained the stain including those areas detected by vulvoscopy, were selected for biopsy. The vulva was cleansed with antiseptic solution and 1% lignocaine was injected into the skin using a dental syringe.

These areas were then excised using a scalpel and sutures inserted where necessary. All specimens were sent in formalin for histopathological assessment. This was then followed by colposcopic assessment of the vagina and cervix and
all abnormal areas were similarly biopsied. Patients were given post operative analgesia as well as antiseptic cream [Povidine- Iodine] to apply to the biopsied areas. A follow up visit was arranged 3 weeks later at which the histology results and further management was discussed with the patients.

1. RESULTS

The findings of this descriptive study were analyzed by a qualified statistician attached to the University of Natal Medical School, and are as follows:

1.1 CLINICAL FEATURES

This study covered a period of 18 months and included 62 patients in total. The mean age of the patients was 47.2 years [range 6 – 73]. The mean parity was 2.5 [range 0 – 4]. The commonest presenting symptom was pruritus vulvae [70%] [Table]. Only 18% of patients reported the presence of a white vulval skin lesion. In a small percentage of patients [1.7%], these lesions were detected on routine gynaecological examination.

The majority of patients [94%] did not have similar lesions elsewhere in the body, whilst 5% of patients also had similar skin lesions involving the trunk, limbs and abdomen in addition to the vulval lesion. In 43% of patients, the white skin involved the vulva and perineum with relative sparing of the area in-between. This type of skin lesion was called the "Figure of 8" pattern. The
remainder of the patients had white skin lesions involving the clitoris, labia majora, labia minora, posterior fourchette and perineum, alone or in combination.

1.2 INVESTIGATIONS

The majority of patients [n=47] had a benign pap smear of the cervix, whilst 5 patients had human papillomavirus infection detected on pap smear. Two patients had mild cervical intraepithelial neoplastic lesions [low-grade squamous intraepithelial lesion] detected on smear and 2 patients had acetowhite areas of the vulva detected on vulvoscopy.

Two patients had mild to severe grade cervical intraepithelial neoplastic abnormalities detected on colposcopy. There were no abnormalities detected on colposcopy of the vagina and no premalignant or malignant abnormalities of the vulva. The Collin’s test was positive in 40% of patients and the commonest area in which this test was positive, was the posterior fourchette, where it was noted that many of these patients had fissures. [Table II]

1.3 HISTOLOGICAL FEATURES

The commonest histological diagnosis was lichen sclerosus in 70% of patients, with squamous cell hyperplasia being the second commonest histological finding. [20%] Of the remaining patients, 9% had non –
specific dermatitis and 1.7% had lichen simplex chronicus. None of the patients had vulval intraepithelial neoplasia or invasive carcinoma of the vulva. [Table III]

The commonest histological diagnosis across all age groups was lichen sclerosus. Those patients who had white skin lesions involving other sites of the body also had lichen sclerosus when it was also present on the vulva. [N = 3] On comparing the pattern of white vulval skin distribution with histological diagnosis, it was found that those patients who had white skin lesions in a “Figure of 8” distribution, also had lichen sclerosus on histology.

Two patients had cervical intraepithelial neoplasia [CIN] diagnosed histologically. The 2 patients who had acetowhite areas detected on vulvoscopy where found to have features of human papillomavirus infection histologically.
CHAPTER 4

1. DISCUSSION

The present study done over an 18 month period included 62 patients in total, all of whom were of the Asiatic race group. Previous studies have found that most of the vulval dermatoses tend to occur mainly in Caucasian groups, although, it has been documented in Black patients by Barclay et al [1966] and Dogliotti et al [1974]. Meyrick – Thomas et al [1987] found lichen sclerosus to occur in 1% of Asian women in a study involving 350 patients, although, here the study population consisted mainly of White females. The reason for this racial predilection is as yet unknown.

Although RK Khan Hospital is situated in an area, which drains predominantly Indians patients, many Black patients from surrounding areas attend the hospital for medical attention.

The distribution of the patients with regards age varied widely with most of this variation being accounted for by lesions detected in premenarchal girls with lichen sclerosus. Only 7 patients [11%] were under the age of 30 years. The majority of patients were above the age of 50 years and the mean age of all patients was 47.2 years. The occurrence of lichen sclerosus in prepubertal females as well as postmenopausal females is similar to that reported by Kaufman et al [1994]. Majority of the patients with
squamous cell hyperplasia were under the age of 50 years, in keeping with that reported by Kaufman et al [1994].

The parity of all patients studied ranged from 0 – 4 and greater, whilst the mean parity was 2.5. There is no evidence from the literature that there may be any relationship between parity and the occurrence of white vulval skin lesions.

Only 18% of patients reported the presence of a white vulval skin lesion. Here the lesion was either detected by their general practitioner or in a few cases by the patients themselves. Most patients who noted the lesions themselves did not present immediately. Reasons for this varied. Some patients were embarrassed and therefore did not seek medical opinion, whilst others thought that the lesion was harmless. This was in spite of the fact that most of these lesions were associated with troublesome pruritus vulvae. The presenting complaints varied with pruritus vulvae being the most frequent [70%]. A very small percentage [1.7%] of patients were asymptomatic. These findings are in keeping with that reported by Kaufman et al [1994]. This stresses the need to carefully examine the vulva at every gynaecological examination to detect asymptomatic lesions. It has been shown that the prognosis of vulval malignancies is better the earlier the lesion is detected. There were 3 patients[5%] who had white skin lesions
involving the genitalia as well as extragenital sites. These lesions were usually detected at routine examination. These findings concur with that of Kaufman\[39\] et al [1994] who found the incidence of lichen sclerosus in extragenital sites to be 3\% in 200 women with genital lichen sclerosus.

White skin lesions can involve any site of the vulva. Whilst 43\% of patients had the so called "figure of 8" type distribution of white skin lesions, where the lesion involved the vulva and perineum with relative sparing of the area in-between, the majority of the remaining patients had white skin distribution involving multiple random sites with no particular pattern. Although the "figure of 8" pattern is classical of lichen sclerosus, some patients with varied pattern of white vulval skin distribution, also had lichen sclerosus on histology. Thus, the clinical appearance of the white skin distribution correlates with that described in the literature, with the exception that no patients in the study with lichen sclerosus had phimosis or clitoral stenosis. These features emphases the point that a diagnosis cannot be made by simply inspecting the lesions macroscopically.

Vulvoscopy was done using a standard colposcope used for microscopic examination of the cervix. Generally most lesions were covered with keratin and only 2 patients had colposcopic evidence of human papilloma virus infection, which was confirmed histologically. The limitation of vulvoscopy
due to keratin has been reported by Reid [111] et al [1995]. In some patients KY jelly was applied to the skin to reduce the reflection of the light from the colposcope. However, there seemed to have been little improvement in this respect. There were no specific vulvoscopie patterns noted in patients diagnosed with vulval dermatoses.

The Collin’s test was positive in 40% of patients and the posterior fourchette was the most common area to stain positive. Here it was noted that majority of patients had fissures present which could have followed on scratching or intercourse. It was noted histologically that those patients with positive staining of the posterior fourchette had lichen sclerosus present. However, this does not imply that the commonest site to find lichen sclerosus is the posterior fourchette, as lichen sclerosus was also detected at other sites. This is in keeping with the observations of Collin that areas devoid of epithelium, exposing nuclear material would stain positive with application of toludine blue. Some would interpret this findings as being “false positives”.

However, Collin [14] [1966] stated that this test is not a test to detect areas with malignancy, but to select sites for biopsy in order to exclude malignancy histologically. If random sites are biopsied without doing vulvoscopy or the Collin’s test, significant areas could be missed where premalignant or malignant disease is present. These conditions frequently tend to be multicentric and therefore the determination of the extent of the disease is
vital to guide therapy. The histopathologists are also faced with a problem when large random specimens are sent to them for assessment, as it may be difficult to decide which part of the specimen to choose for histological assessment.

Histological findings showed that lichen sclerosus was the commonest diagnosis [70%] across all age groups, in keeping with that reported in the literature [17]. The histological features supporting the diagnosis of lichen sclerosus included: hyperkeratosis, epithelial thinning, flat or absent ret pegs, follicular plugging, a homogenous acellular area beneath the epidermis and an inflammatory cell infiltrate in some cases. Friedrich [17] [1983] also reported that lichen sclerosus was the commonest cause of white vulval skin lesions, occurring in 70% of patients.

There were 13 patients with a histological diagnosis of squamous cell hyperplasia. The features supporting this diagnosis included hyperkeratosis, acanthosis or epithelial thickening, elongation and distortion of the rete pegs and a chronic inflammatory cell infiltrate in the dermis. None of these patients had any underlying dermatosis, which could have resulted in these changes. The diagnosis of squamous cell hyperplasia was therefore made by exclusion, as recommended by Wilkinson [46] [1992].
Six patients in the study had non-specific dermatitis diagnosed histologically. Histologically, it was found there were no specific features to arrive at a specific diagnosis. The features consisted mainly of inflammatory cells as well as perivascular inflammation in some cases. Non-specific dermatitis as the histological finding in some patients with white vulval skin lesions, is not commonly reported in the literature. O'Keefe et al [1995] found the incidence of non-specific dermatitis to be 6% in 114 patients studied.

There were no patients in the study with vulval intraepithelial neoplasia or vulval invasive carcinoma. Of note is that the biopsy specimens were either taken from areas found to stain with toluidine blue or random sites when the Collin's test was negative. In view of the negative vulvoscopy findings as well as negative histological findings of those areas biopsied when the Collin's test was positive, the role of vulvoscopy and the Collin's test may be questioned. However, it must be remembered that the aim of these tests is to select areas to biopsy to exclude malignant or premalignant lesions histologically and not to diagnose such lesions by these tests directly.

The findings in this study confirm the fact that there are many different causes of a white vulval skin lesion. Since the treatment of the different causes of white vulval skin lesions vary from medical to surgical, with surgery
having its attendant problems, it is imperative that clinicians treat these lesions based on histological findings.

2. CONCLUSIONS AND RECOMMENDATIONS

A plethora of terms have been applied to lesions of the vulva, characterized by shrinkage, whitening or reddening. Many such terms were used interchangeably as clinical and histological descriptions. The looseness of such terminology led to a wide variety of therapeutic modalities such as surgery and radiotherapy, for conditions or unproven malignant potential. The present study shows that the majority of white vulval skin lesions are benign in nature. This has been the reason why there has been uncertainty in the past as regards the approach to these patients. There has been a tendency to treat empirically without doing any investigations.

The approach adopted in this study and which is therefore recommended should be to do a Pap smear, vulvoscopy, vaginoscopy, colposcopy, Collin’s test and directed biopsies of abnormal areas detected by these tests. In spite of the limitations of these tests, we can expect premalignant areas to be detected if they are present in a patient. The value of these tests is akin to the practice of doing colposcopy and directed biopsies of the cervix if a patient has an abnormal pap smear. Here, the implications are similar if a
premalignant or malignant lesion is diagnosed in addition to the fact that prognosis is better the earlier the diagnosis is made.

IN SPITE OF THE LIMITATIONS OF THESE TESTS AND THE FACT THAT NO PATIENT IN THIS STUDY HAD PREMALIGNANT OR MALIGNANT LESIONS, MY RECOMMENDATION TO DO THESE TESTS CONCURS WITH THAT OF LEADING VULVOLOGISTS. [17, 19, 91]
**TABLE I: PRESENTING COMPLAINTS**

<table>
<thead>
<tr>
<th>Complaint</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritus vulvae</td>
<td>43</td>
<td>[70%]</td>
</tr>
<tr>
<td>White vulval skin</td>
<td>11</td>
<td>[18%]</td>
</tr>
<tr>
<td>Vaginal discharge</td>
<td>21</td>
<td>[36%]</td>
</tr>
<tr>
<td>Post menopausal bleeding</td>
<td>1</td>
<td>[1.7%]</td>
</tr>
<tr>
<td>Hot flushes</td>
<td>2</td>
<td>[3.4%]</td>
</tr>
<tr>
<td>Generalized white skin of body</td>
<td>1</td>
<td>[1.7%]</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>1</td>
<td>[1.7%]</td>
</tr>
</tbody>
</table>
TABLE II: RESULTS OF COLLIN’S TEST

| Negative | 35  | [60%] |
| Positive | 23  | [40%] |

<table>
<thead>
<tr>
<th>No. of Positive Areas</th>
<th>Site</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Lower labia majora</td>
<td>Lichen sclerosus</td>
</tr>
<tr>
<td>13</td>
<td>Posterior Fourchette</td>
<td>Lichen sclerosus</td>
</tr>
<tr>
<td>3</td>
<td>Posterior Fourchette</td>
<td>Squamous cell hyperplasia</td>
</tr>
<tr>
<td>2</td>
<td>Right/left labia majora</td>
<td>Lichen sclerosus</td>
</tr>
<tr>
<td>1</td>
<td>Clitoris</td>
<td>Squamous cell hyperplasia</td>
</tr>
<tr>
<td>2</td>
<td>Posterior Fourchette</td>
<td>Non-specific dermatitis</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Count</td>
<td>Percentage</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>-------</td>
<td>------------</td>
</tr>
<tr>
<td>Lichen Sclerosus</td>
<td>43</td>
<td>70%</td>
</tr>
<tr>
<td>Squamous Cell Hyperplasia</td>
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<td>20%</td>
</tr>
<tr>
<td>Non-specific Dermatitis</td>
<td>5</td>
<td>9%</td>
</tr>
<tr>
<td>Lichen Simplex Chronicus</td>
<td>1</td>
<td>1.7%</td>
</tr>
<tr>
<td>Vulval Intraepithelial Neoplasia</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Vulval Carcinoma</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
PHOTOGRAPH NUMBER 1

CLINICAL FEATURES OF LICHEN SCLEROSUS

Photograph shows white vulval skin in a background of normal skin.

Note the peri-introital and peri-anal involvement.
PHOTOGRAPH NUMBER 2

CLINICAL FEATURES OF SQUAMOUS CELL HYPERPLASIA

Photograph shows white vulval skin lesion involving multiple areas of the vulva with no particular pattern.
FIGURE 1

CLINICAL FEATURES OF LICHEN SIMPLEX CHRONICUS

Figure shows white leathery appearing vulval skin
FIGURE 2

CLINICAL FEATURES OF LICHEN PLANUS

This figure shows the erosive type of lichen planus as can be seen in the region of the introitus where there is desquamation of the skin. The skin surrounding this region appears white in colour. There is also a purplish-white skin lesion noted in the surrounding areas which is typical of lichen planus.
PHOTOGRAPH NUMBER 3

HISTOPATHOLOGICAL FEATURES OF LICHEN SCLEROSUS
PHOTOGRAPH NUMBER 4
HISTOPATHOLOGICAL FEATURES OF SQUAMOUS CELL HYPERPLASIA
PHOTOGRAPH NUMBER 5

HISTOPATHOLOGICAL FEATURES OF LICHEN SIMPLEX CHRONICUS
FIGURE 3

CLINICAL FEATURES OF VULVAL INTRAEPITHELIAL NEOPLASIA

The figure shows white vulval skin lesion with areas of plaque formation in a patient with vulval intraepithelial neoplasia.
PHOTOGRAPH NUMBER 6
HISTOPATHOLOGICAL FEATURES OF VULVAL INTRAEPITHELIAL NEOPLASIA
FIGURE 4

CLINICAL FEATURES OF PAGET'S DISEASE OF THE VULVA

The figure shows white vulval skin lesion scattered over a bright red base, typical of Paget's disease of the vulva.
PHOTOGRAPH NUMBER 7

HISTOPATHOLOGICAL FEATURES OF PAGET'S DISEASE OF THE VULVA
FIGURE 5

CLINICAL FEATURES OF INVASIVE SQUAMOUS CELL CARCINOMA OF THE VULVA

White vulval skin with areas of nodularity. This lesion cannot be clinically differentiated from the other causes of white vulval skin lesions.
PHOTOGRAPH NUMBER 8

HISTOPATHOLOGICAL FEATURES OF INVASIVE SQUAMOUS CELL CARCINOMA OF THE VULVA
PHOTOGRAPH NUMBER 9

THE COLPOSCOPE
FIGURE 6
KEYES CUTANEOUS PUNCH BIOPSY INSTRUMENT
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