

8. Differential Diagnosis.

Certain other conditions may occasionally resemble oral lichen planus very closely.

(a) Leukoplakia.

Cooke points out that leukoplakia is commoner in men, there is no history of remissions, that the commissures are often involved, and there are no patterns. Darling and Crabb (1954) comment that the plaque-like lesions of lichen planus are hard to distinguish from leukoplakia, but that individual papules and striae may be seen at the periphery. If there is considerable hyperkeratinization, the coalescence of papules to form a plaque may obscure the true nature of the lesion, and it may not always be possible to differentiate the lesion from leukoplakia. If skin lesions are present, the probability is that the oral lesion is lichen planus also, but it does not exclude the possibility of leukoplakia. These authors quote a case of Sayer in which there was a characteristic lichen planus on the right buccal mucosa, and a plaque on the left buccal mucosa was biopsied and reported as leukoplakia. Where there is doubt, biopsy is indicated. Leukoplakia shows more marked hyperkeratosis, the acanthosis is relatively greater, the inflammatory infiltrate is not so closely confined to the basal cell layers, while plasma cells and mast cells may be numerous in leukoplakia, they are rare in lichen planus. Both Darling and Crabb, and Cooke, point out that it is only in leukoplakia that transitional changes between hyperplasia and neoplasia are seen in the epithelium, although Rushton and Cooke (1963) state that in atrophic lichen planus

such changes are a remote possibility. The dryness of leukoplakic lesions serves to differentiate them from lichen planus (Cawley and Kerr, 1952).

Shafer, Hine and Levy (1963) do not find any difficulty in the differentiation of the two diseases, as they state that the clinical characteristics are usually sufficient, and that if biopsy is necessary, the microscopic picture of lichen planus is characteristic and pathognomonic.

Burket (1961) has observed patients having coexisting leukoplakia and lichen planus of the oral mucosa, which have been verified histologically.

McCarthy and Shklar (1964) state that there must be a correlation of both clinical and microscopic evidence. Many authors emphasize the importance of biopsy in lichen planus to rule out the potentially more serious leukoplakia.

(b) Syphilitic Mucous Patches.

These can be distinguished from lichen planus by their inflammatory halo, lymphadenitis, positive serological tests (Cawley and Kerr, Darling and Crabb, Cooke), by the fact that they favour the commissures of the lips and the tonsils (Cooke), and by the friability of mucous patches (McCarthy and Shklar).

The latter authors also point out that the atrophic glossitis of tertiary syphilis may resemble the atrophic form of lingual lichen planus very closely. Biopsy usually reveals a sclerotic vascular picture in syphilitic glossitis, as well as perivascular lymphocytic infiltration.

(c) Moniliasis.

All authors are agreed that lichen planus can easily be differentiated from moniliasis by the facts that in the latter the white patches can easily be scraped off, leaving a bleeding surface, and microscopic examination of the scrapings will show the fungus. Burket (1961) points out that history of recent antibiotic therapy will help in the differential diagnosis.

(d) Aphthous Ulcers.

Cooke, Darling and Crabb, and Burket agree that the white papules and streaks of lichen planus, and transitory nature of the aphthae will be diagnostic.

(e) Benign Mucous Membrane Pemphigoid.

McCarthy and Shklar state that, when bullous lichen planus occurs, differentiation may be quite difficult. Lichen planus does not involve the ocular mucous membranes, and at the periphery of the erosive areas, there are definite infiltrative lesions in lichen planus which are absent in mucous membrane pemphigoid.

(f) Pemphigus Vulgaris.

Cooke points out that the bulla in pemphigus occurs on a normal appearing mucosa, not a papular one, and that the presence of acantholytic cells in a scraping from the bulla is diagnostic. McCarthy and Shklar make the distinction that in pemphigus the vesicles are intraepithelial, but in lichen planus, always subepithelial.

(g) Lupus Erythematosus.

Distinguishing features are pointed out by :-

Cawley and Kerr - the lesions are red, have no lace-like lesions, leave residual scars.

Cooke - the area of atrophy and scarring remains stationary over many months or years, and is firm on palpation. Microscopically the infiltration is mainly in the middle and deeper layers of the dermis, and may contain plasma cells.

Darling and Crabb (1954) - reddened scaling patches on the face, ears and scalp usually accompany the skin lesions; the oral ulcers have a reddish border and a yellowish centre which tears away leaving a bluish-red epithelium.

McCarthy and Shklar - the microscopic features are helpful, these being parakeratosis, hydropic degeneration of the basal layer, some degeneration of the connective tissue collagen, while the chronic inflammatory infiltrate tends to be perivascular rather than sub-epithelial. These latter remarks apply to chronic discoid lupus erythematosus.

(h) Erythema Multiforme.

McCarthy and Shklar mention that this disease in certain cases resembles bullous lichen planus. Careful evaluation of the history and biopsy findings are of value, together with the severe involvement of the labial mucosa and the acute nature of erythema multiforme.

(i) Fordyce's Spots.

Cooke states that these may be similar to the discrete papular type of lichen planus, and that biopsy is diagnostic.

9. Special Topics.

Lichen Sclerosis et Atrophicus.

Only two authors have been found in the literature who mention this condition - Orban and Wentz (1960), and McCarthy and Shklar.

The latter are not convinced that the oral lesions described as accompanying this disease were those of lichen sclerosis et atrophicus, and doubt their actual occurrence at all. The microscopic features have not been sufficiently clear-cut to render a definitive diagnosis rather than lichen planus or even leukoplakia.

Orban and Wentz appear to have no doubt that oral lesions do occur, and that the disease is a completely different entity from lichen planus. Lesions are commonly limited to the vulva, perioral areas and penis. The genital lesions often present patches of leukoplakia and may progress to carcinoma. Ravits and Welsh reported three cases confined to the mouth. The microscopic appearance was; sclerotic connective tissue, lymphocytic and histiocytic infiltration, and atrophic epithelium with complete absence of epithelial ridges, and some hyperkeratosis.

Lichen Planus and Pigmentation.

Cooke describes a pigmented pattern of brown papules and plaques on the posterior aspects of both cheeks. White keratinized areas occurred in the centre of the brown patches and independently of them. Stones (1962) mentions similar lesions, but it is not clear from his text whether he is reporting Cooke's observations or his own.

McCarthy and Shklar's observations regarding pigmentation apply to that occurring following oral lesions. They state that it is extremely rare, and that they have seen only one case involving the soft and hard palate.

Lichen Planus and Psoriasis.

McCarthy and Shklar have seen the association of oral lichen planus with psoriasis of the body in only one case, and state that the relationship is probably coincidental.

Lichen Planus and Oral Malignancy.

Cawley and Kerr state that carcinomatous changes have been described, but must be exceedingly rare. Warin et al (1958) described one patient who developed an epithelioma on the site of recurrent ulceration of the buccal mucosa of 13 years duration. Warin (1961) described an earlier (1960) report of 45 cases, 4 of which had later developed an epithelioma, and 2 had thickened white patches with the histologic characteristics of leukoplakia, nearly always at the site of repeated ulceration. Later, 2 more cases of epithelioma associated with lichen planus were seen, and one of the previously reported leukoplakias developed an epithelioma. Thus it appeared that 1 in 10 cases of oral lichen planus, epithelioma or leukoplakia had developed. Cahn and Slaughter (1962) state that in recent years they have seen two cases of oral lichen planus, diagnosed as such by competent pathologists, that eventually developed into carcinoma. They have, therefore, become more sceptical of the diagnosis, particularly if there are no concomitant skin lesions.

McCarthy and Shklar aver that the development of carcinoma related to lichen planus is extremely rare. They quote Lottes et al as reporting four cases of malignancy arising in erosive lesions of lichen planus, and pointing out the rarity of this association, but cast some doubt on the classically accepted benignity of oral lichen planus.

Lichenoid Stomatitis of Atabrine.

Various authors quote the study by Bazemore et al which showed that lesions of lichen planus or similar to lichen planus were found to occur on the skin and oral mucosa following the use of Atabrine, the most typical oral lesions being a lace-like type on the buccal mucosa and an atrophic glossitis. The microscopic picture was also compatible with lichen planus.

10. Therapy.

Various authors recommend treatment as follows:-

Cawley and Kerr; Varied treatments have been recommended, including the use of arsenicals, bismuth and mercurials.

Cooke (1954); Reassure the patient that no malignancy is present, recommend biopsy in atypical cases. Relieve irritation from sharp edges. For acute cases, 2% aureomycin mouthwashes may be used, secondary infection may be controlled by painting with 1% aqueous gentian violet.

The results of treatment are hard to assess, because of natural remissions, but treatment that effectively controls lichen planus of the skin does not affect the oral lesions.

Darling and Crabb (1954); The treatment is empirical. General treatment is aimed at increasing the general health. Attention should be given to hygiene, a plain diet, and freedom from anxiety; focal infection should be eliminated. The effects of suggestion in the various forms of treatment cannot be discounted.

Ayres and Ayres (1955); Chloroquine was effective in some cases, but not in others. The high incidence of potentially serious side-effects, dizziness, visual and gastro-intestinal disturbances, and blood dyscrasias, must be considered.

Warin et al (1958); There is no specific treatment. Explanation, reassurance, simple psychotherapy, sedatives, supportive treatment may be helpful.

Bernier (1959); Mercury or arsenic preparations are of benefit, while Fowler's solution and mild X-ray irradiation have been suggested. More important is good oral hygiene, plenty of rest and sunshine, relief from worry.

Orban and Wentz (1960); Local treatment is palliative. Adequate rest is advised, and avoidance of the excessive use of coffee, tea, alcohol and tobacco. For very depressed patients, psychiatric treatment may be necessary. The use of Fowler's solution, sodium bismuth triglycollate, vitamins A and D, X-ray therapy and cortisone have been recommended.

Warin (1961); Trauma and irritation from dentures, sharp teeth and smoking should be reduced, particularly in cases with recurrent ulceration.

Burket (1961); Reassurance is needed, tranquillizers may be

helpful, and psychotherapy may be indicated if cancer-phobia is fixed. Buccal vitamin A may be helpful.

For bullous lesions anaesthetic troches or solutions may be prescribed for symptomatic relief when pain is severe. A mild antimicrobial agent may be used.

Stones (1962); Reassurance is important; for ulceration, 1% Gentian violet is applied, or a mouthwash containing 3% chlortetracycline and 10% glycerine is helpful to treat secondary infection, but no treatment is known that cures the oral lesion.

Shafer, Hine and Levy (1963); Reassurance as to benignity is very important, since many of the patients are cancer-phobic. There is no specific treatment.

McCarthy and Shklar (1964); Treatment is unsatisfactory. Usually no treatment is indicated. When discomfort is severe with the bullous form, corticosteroid therapy both topically and systematically will give symptomatic relief.

Because the emotional state of the patient is important, tranquillizers may be of some value. Reassurance is most important, as a high percentage of patients have cancerophobia. Since lichen planus is self-limiting, time is in favour of the clinician, and patience will eventually be rewarded by a spontaneous cure.

Psoriasis.

1. Introduction,
2. Clinical Features,
 - (a) Cutaneous Manifestations,
 - (b) Oral Manifestations.
3. Aetiology,
4. Histologic Features,
5. Treatment.

1. Introduction.

Psoriasis is a rather common chronic inflammatory disease, which in rare instances is reported to manifest oral mucous membrane lesions.

Most authorities consider oral mucosal lesions to be very rare, and point out that oral lesions concomitant with psoriasis of the skin are actually other diseases such as leukoplakia or lichen planus. In fact, some investigators deny the existence of oral psoriasis, and information in the dental literature is relatively scarce. Nevertheless, it has been reported that in occasional cases oral lesions have exhibited all the histologic features of psoriasis, and in some instances, have been identical with the co-existing skin lesions.

Levin (1954) stated that Bernier and many other authorities are of the opinion that oral psoriasis is nothing more than leukoplakia in one of its varying stages of pathology. Bernier (1959) however, devotes a section to psoriasis and describes the features of the oral lesions.

2. Clinical Features.

(a) Cutaneous Manifestations.

Small, sharply delineated, dry papules occur, each covered with a delicate, silvery scale, described as resembling a thin layer of mica. If deep scales are removed, one or more tiny bleeding points are disclosed, a characteristic feature termed Auspitz's sign. After removal of the scale, the surface of the skin is red and dusky in appearance. The lesions, painless and seldom pruritic, may be few in number or extensive in distribution. The papules enlarge at the periphery and tend to become slightly infiltrating and elevated, the smaller lesions coalescing to form large plaques of irregular outline. The lesions are roughly symmetrical, are most frequently grouped on the extensor surfaces of the extremities, particularly the elbows and knees, the scalp, back and chest, face and abdomen. Involvement of the hands and feet, with the exception of the fingernails, is uncommon. The disease may remain static for a long time, progress slowly, or exhibit acute generalized exacerbations. Warm weather usually brings an improvement. Arthritis is a complication in about 12% of cases, according to Allen. The disease arises most frequently in the second and third decades; there is no sex predilection, (Shafer, Hine and Levy).

(b) Oral Manifestations.

Brayshaw and Orban (1953) described three cases of psoriasis of the gingivae, a site of involvement not previously reported. The lesions were small plaques. In one case, the lesions were bilateral and symmetrical. In all cases the surface was irregularly covered

by small, silvery scales. Tiny bleeding points appeared on scraping the surface with a dull instrument. There were no subjective symptoms other than a vague itchy feeling.

Oral lesions have been reported on the lips, buccal mucosa, palate, gingiva and floor of the mouth. They have been described as grey or yellowish-white plaques; as silvery-white scaly lesions with an erythematous base; as multiple papular eruptions which may be ulcerated; or as small, papillary, elevated lesions with a scaly surface. Reports by Goldman and Bloom (1951) and by Levin (1954) emphasized the vagaries of the clinical appearance of oral psoriasis. Brayshaw and Orban's patient with psoriasis of the gingiva did not have skin lesions, however, Shafer, Hine and Levy emphasize that cases of mucosal involvement without skin manifestations must be viewed with caution, even though the histologic sections of the lesions do present a psoriaform pattern.

Levin reported that the lymph nodes may be involved.

Burket (1961) asserted that diagnosis is extremely difficult if not impossible on the basis of the clinical lesion alone. Biopsy examination is required.

3. Aetiology.

Most writers agree that the cause of psoriasis is unknown, but some speculations have been made:-

Levin; Psoriasis may be due to a constitutional disturbance of fat-soluble vitamin metabolism, or perhaps to an allergic manifestation of fungus infection. There are theories of familial tendencies, focal infection and climatic disturbances. The patient is usually a

healthy individual otherwise.

Cheraskin and Langley (1956); There is a definite familial tendency in 30% of cases.

Bernier; Theories are that psoriasis may be a direct infection, or the effect of an allergen. In 30-35% of cases, there appears to be a familial pattern.

Stones (1962); There is a familial incidence in about 30% of cases.

Shafer, Hine and Levy; Heredity is reported to be a factor in some cases, but these are exceptional. Infection by various micro-organisms, metabolic disturbances, endocrine dysfunction and neurogenic factors have been considered important, although with little factual basis. Mental anxiety or stress almost invariably appears to increase the severity of the disease or induce acute exacerbations.

4. Histologic Features;

Brayshaw and Orban described these as follows:-

1. Parakeratosis, 2. Elongation and clubbing and lacy fusion of the epithelial ridges and rete pegs, 3. Thinning of the supra-papillary part of the epithelium so that often only a parakeratotic layer covers the papilla, 4. Widening of the tip of the connective tissue papillae due to inflammation, widening of the capillaries, and oedema, 5. The presence of micro-abscesses located in the parakeratotic layer of the epithelium.

Levin's description included perivascular infiltration of round cells, and fibroblastic invasion of the papillary zone of the corium.

Bernier described alternating areas of hyperkeratosis, particularly in the acute form, and found that there was no oedema of the connective tissue papillae.

Orban and Wentz (1960) commented that the presence of air spaces in the lamellae between the parakeratotic surface cells accounts for the clinical appearance of the silvery scales.

Shafer, Hine and Levy found that intraepithelial micro-abscesses (Monro's abscesses) are a common but not invariable finding; mild lymphocytic and histiocytic infiltration of the connective tissue is also typical.

5. Treatment.

Bernier stated that treatment is difficult. When no complicating factors exist, no special therapy is indicated. When infection is prominent it must be cared for. Bland mouthwashes and good oral hygiene are of great importance. The application of gentian violet in mild solution may be advantageous.

Orban and Wentz recommended consultation with a dermatologist, limitation of the use of alcohol, and vitamin A, 150,000 units per day. Vitamin B complex and crude liver extract have shown beneficial effects. Vitamin D₂ has also been recommended. Cortisone and A.C.T.H. are effective in temporarily alleviating the symptoms. The intravenous injection of Maphuride sodium has been reported to cause an improvement. Patients presenting with only gingival lesions have had no recurrence after complete excision.

Stones stated that tar preparations, irradiation and ultra-violet therapy are of value. Systemic therapy is usually ineffective.

Relapses frequently occur.

Shafer, Hine and Levy state that any relief by the use of lotions, ointments and ultraviolet light is only symptomatic and temporary. Psoriasis is cosmetically disfiguring, but innocuous, having no serious consequence.

Lupus Erythematosus.

Lupus erythematosus is the most common of the "collagen diseases". This term is confusing since it is in the entire connective tissue that the pathologic changes are noted. The term "fibrinoid", also freely used in the histologic description of collagen diseases, was generally thought to be a special form of degeneration of connective tissue. Recent studies with electron microscope have indicated that fibrinoid appears to be fibrinogen which has in some way been precipitated in the tissues, (McCarthy and Shklar, 1964).

Lupus erythematosus will be considered under the following headings:-

1. Classification.
2. Occurrence.
3. Aetiology.
4. Clinical picture.
 - (a) Chronic discoid,
 - (b) Acute disseminated,
 - (c) Subacute disseminated.
5. Histopathology.
 - (a) Chronic discoid,
 - (b) Acute disseminated.
6. Diagnosis.
 - (a) Chronic discoid,
 - (b) Acute disseminated.
7. Differential diagnosis.
 - (a) Chronic discoid,

Lichen planus, leukoplakia.

(b) Acute disseminated.

Mucous membrane pemphigoid, syphilis.

8. Therapy.

(a) Chronic discoid,

(b) Acute disseminated.

1. Classification.

This is probably the most critical point in evaluating the disease lupus erythematosus, as a proper understanding of the various types is vital to intelligent determination of the diagnosis and prognosis.

Cheraskin and Langley (1956), McCarthy and Shklar (1958) and Bhaskar (1961) classify the disease into two types; the acute disseminated form and the chronic discoid form. Thoma and Goldman (1960) use this classification and also state that acute and sub-acute forms of the disseminated type may occur.

Cook (1958) and McCarthy and Shklar (1964) classify lupus erythematosus into three types; acute disseminated, subacute disseminated and chronic discoid.

Sugarman (1953), Stones (1962) and Shafer, Hine and Levy (1963) divide the disease into four types; acute disseminated, sub-acute disseminated, chronic disseminated, and chronic discoid.

Sugarman quotes Andrews as suggesting that the acute disseminated and chronic discoid forms bear "little kinship and may be completely unrelated", while Shafer, Hine and Levy also mention the possibility. However, McCarthy and Shklar "feel strongly that

one pathologic process is in operation and that the differences in manifestations are because of 'patient resistance' based perhaps on immunologic, hormonal, or other variations".

2. Occurrence.

Sugarman reports the frequency of oral manifestations in the chronic discoid type according to various workers:-

Monash 50%, Smith 27%, Culver 28%.

Burket (1961) states that lesions of lupus erythematosus occur on the oral mucosa in about 25% of cases, while Shafer, Hine and Levy set the occurrence at 25-50%, commenting that the oral lesions seldom appear first, and that they are also seen occasionally in the disseminated form. McCarthy and Shklar state that the incidence of oral involvement varies, depending upon the acuteness of the disease. While not more than 10% of the chronic discoid type present oral lesions, as many as 75% of the acute disseminated type have some oral manifestation before death. Lupus erythematosus may occur on the oral mucous membrane without skin lesions in extremely rare instances.

Most authors agree that chronic discoid lupus erythematosus is a relatively common disease, and that it ranks high in chronic mucocutaneous disorders. The disseminated forms are much less common and usually involve only females.

McCarthy and Shklar comment that much confusion can accompany any attempt to give strict percentages in relation to the site of involvement, because of variations in the methods of individual studies. They state that mucous membrane involvement in chronic

discoid lupus erythematosus is seen less commonly than the cutaneous lesions. In the disseminated variety, the oral mucosa is a frequent area of involvement and the oral lesions are particularly prominent as the disease approaches a fatal termination. In these instances the clinical picture is nonspecific and may represent merely a necrosis of mucosal epithelium secondary to neutropenia.

3. Aetiology.

The cause is unknown. Many theories have been advanced, but none has been substantiated. Tubercular origin was attributed to lupus erythematosus for many years, but there is no evidence to incriminate the tubercle bacillus in any way in the development of lupus erythematosus, (Stones, McCarthy and Shklar).

Extensive search has been made with many patients in an attempt to uncover a focus of infection in the form of an alveolar abscess, chronic prostatitis, sinusitis, tonsillitis, etc. Elimination of the focus of infection, when found, rarely affects advantageously the course of the disease, (McCarthy and Shklar). Cook seems to think that focal infection does play a part, as he states that eradication of foci of infection is a valuable measure in discoid cases, but dangerous in the disseminated type. Sugarman, Burket and McCarthy and Shklar mention that photosensitivity, while not the actual cause, is certainly a precipitating factor in exacerbations of at least the skin lesions, and may also influence the general course of the systemic varieties.

Recently, much interest has centred around the

"immunologic" approach, and the possible "auto-immune" mechanism has been given much consideration. In view of the phenomenon of the L.E. test, it must be admitted that the greatest opportunity for fruitful investigation undoubtedly lies in the field of immunology, (McCarthy and Shklar).

4. Clinical Picture.

(a) Chronic Discoid Lupus Erythematosus.

This is a purely mucocutaneous disorder and affects either sex, with a slight predominance of females, appearing at any age, but usually seen first between the ages of 20 and 40. It is unlikely to develop for the first time after the sixth decade.

The natural course of the disease is one of pronounced chronicity, with chances of remissions and exacerbations. However, there is a tendency for gradual remission, and eventually many cases become "burned out" over a period of years. Considerable scarring may result; thus it is important that an early diagnosis be made and appropriate therapy begun.

There are no associated signs or symptoms of systemic involvement, and the experience of McCarthy and Shklar is that the chronic discoid type does not progress to disseminated forms. Where reported, a careful review usually indicates that the disease was systemic from the start, and failure to study the patient adequately was responsible for the faulty classification.

Mucous membrane lesions; There is general agreement that the buccal mucosa is the most common site for intra-oral lesions; the

lips also being a frequently described location, possibly representing direct extension from skin lesions. Exposure to light is also responsible for exacerbations in this site, and the lower lip appears to be more severely involved. Any area of the mouth may be involved.

Sugarman describes first an area of bright redness; soon the surface is torn by excoriation, and later shows ulceration. After the red lesion has been present for some time, numerous white lines appear at right angles to the margins. Larger patches show deep central fissures or ulcers. The margins have whitish satellite areas ranging from pin point to pinhead in size. Ormsby and Montgomery (quoted by Sugarman) describe the mature oral lesion as being a well-defined, slightly elevated, superficial patch with a bluish or dark red margin, sloping abruptly toward the centre, and gradually toward the surrounding mucous membrane. At the border are numerous dilated blood vessels having a radial arrangement into the surrounding tissue. When erosions occur they become covered with a smooth, bluish-red epithelium in which are numerous whitish points or lines, or if ulceration intervenes, superficial scarring results. In older lesions, the red border becomes less elevated and is transformed into a white or bluish-white peripheral zone of thickened epithelium. The dilated vessels are replaced by white lines having the same radial arrangement, diverging peripherally. The lesions enlarge by healing in the middle and breaking down at the periphery. They are most often found in the mucobuccal folds, and most often bilaterally.

Stones' description is somewhat similar, but more brief; A typical lesion is that of a red elevated patch, the surface of which soon shows signs of abrasion. At the border are numerous dilated blood vessels having a radial appearance. As the lesion progresses, there is an atrophic change, so that an old lesion has a thin, greyish-white appearance. The blood vessels at the border seem to be replaced by white lines with a similar radial appearance.

Shafer, Hine and Levy state that the oral lesions consist of circumscribed, elevated white plaques, each with a red or purple periphery. Peripheral telangiectasis is also common. Erosion and ulceration often occur, and superficial scarring may result. Frequently the oral lesions resemble leukoplakia, and in the absence of pronounced skin lesions, may be mistaken for the condition. The lesions may or may not be asymptomatic.

McCarthy and McCarthy describe the lesions as well-defined, slightly elevated and infiltrated, with a bluish or dark-red areola. At the border of the lesion, there may be numerous dilated blood vessels having a radial arrangement extending into the surrounding tissue, coupled with whitish pin-head papules. In the early stages, the centre of the lesion is slightly depressed and eroded, and covered with a smooth bluish-red epithelial surface showing scarring. In older lesions, the erythematous border becomes less elevated and is transformed into a whitish or bluish-white peripheral zone of thickened epithelium. The dilated vessels are replaced by white lines having the same diverging radial arrangement. On the tongue, the disease occurs as circumscribed, smooth, reddened areas in which

the papillae are lost, or as patches with a whitish sheen resembling leukoplakia.

McCarthy and Shklar describe the characteristic lesion as a reasonably well-defined area with a somewhat irregular configuration. Increased erythema is prominent, and some loss of epithelium intermingled with patchy hyperkeratosis and exudation is typical. A most striking finding is a unique radial arrangement of capillaries at the periphery, extending into the surrounding tissue. In lesions that have been present for longer periods of time, some scarring may occur and irregular white patches are seen in various areas, both in the centre and at the periphery.

Skin Lesions; Any skin area may be involved, but the most common sites are the face, chest, back and extremities, (Shafer, Hine and Levy).

McCarthy and Shklar state that all the patients they have observed with oral lesions have demonstrated skin involvement. Usually this is quite characteristic and is readily observed over the face, neck, and hands (light exposed areas). The nose and cheeks are classical sites, and involvement of this area is referred to as the "butterfly configuration". Occasionally, one may have to search to discover less conspicuous areas, such as the scalp and ears. Well-defined, erythematous, slightly infiltrated, prominent lesions are the rule. An adherent scale is usually present, and patulent pilosebaceous orifices are present. If the disease is left untreated, disfiguring scarring may occur.

Other descriptions in the literature seem to be quite similar.

(b) Acute Disseminated Lupus Erythematosus.

This is rare, and restricted principally to young females in the later part of the second decade to the early thirties. Except for an unusual case, it runs a fairly rapid course, terminating fatally. The condition may start insidiously with vague symptoms that require prolonged study and observation in order to establish a diagnosis, (McCarthy and Shklar). The systemic manifestations are referable to involvement of various organs, including the kidneys and heart. In the kidney, fibrinoid thickening of glomerular capillaries occurs, producing the characteristic "wire loops", which may be sufficient to result in renal insufficiency. The heart suffers from an atypical endocarditis involving the valves, as well as fibrinoid degeneration of epicardium and myocardium, (Shafer, Hine and Levy).

Mucous membrane lesions; Sugarman states that these are similar to the discoid type, but more acute, with greater destruction. They are irregular, variable, may be ulcerated and have a telangiectatic tendency, being reddish-purple in colour. Healing occurs in the centre, breakdown takes place at the margins. Great variation in the oral lesions exists, and these frequently simulate other diseases.

McCarthy and Shklar comment that the gross pathologic changes described in the chronic discoid variety are rarely observed. Instead there is usually a non-specific picture of bullae, erosions, and necrotic slough. The oral mucosa may merely be reflecting the patient's general condition, as mucosal involvement becomes more

prominent as deterioration advances. Certainly a pronounced leukopenia and general debilitation are sufficient to explain the clinical picture.

Skin lesions; According to Sugarman, there is great variation here. Acute disseminated lupus erythematosus is a systemic disease in which lesions on the skin and mucous membrane are of diagnostic importance only. The skin lesions begin as erythematous patches and coalesce. The face may be oedematous and swollen and the fingers and palms show puffiness and erythematous macules. The "butterfly" appearance across the bridge of the nose and over the cheeks is characteristic. Petechial and ecchymotic spots occur on the trunk and extremities. The clinical picture is complicated by severe renal damage; erythrocytes and large amounts of albumin are present in the urine.

McCarthy and Shklar point out that the skin lesions may be entirely absent throughout the course of the disease. On the other hand, they range from a well-developed discoid variety to an evanescent flushing. Characteristically, they are less well-developed than in the more chronic form and although appearing in the same sites rarely show more than erythema and oedema.

(c) Subacute disseminated lupus erythematosus.

Into this group falls a vague, small group of cases that are difficult to classify either as chronic discoid or acute disseminated lupus erythematosus.

Fairly pronounced skin and mucosal lesions are usually present, similar to the chronic disease. However, some symptoms

such as fever, leukopenia, vague discomforts, and even a positive lupus erythematosus test are frequently observed. This indicates that systemic involvement is present. However, the course is generally benign, with remissions, and the prognosis is much better than with the acute variety.

McCarthy and Shklar feel that this condition represents a low-grade form of disseminated lupus erythematosus, and although the outlook is more promising, a sudden flaring into the acute form may take place unexpectedly.

Chronic disseminated lupus erythematosus: Although, as mentioned earlier, three authors include this category in their classification, the clinical picture is not described.

5. Histopathology.

(a) Chronic Discoid Lupus Erythematosus.

The microscopic features of the oral lesions may be summarised as follows; (1) hyperkeratosis or parakeratosis, (2) hydropic degeneration of the stratum germinativum, (3) a hyaline-like degeneration of connective tissue collagen, and (4) a lymphocytic infiltration arranged in clumps and usually in a perivascular pattern.

Not all descriptions conform exactly however, and the differences will be described for individual authors:-

Sugarman; The epithelium may be atrophic. The rete pegs tend to disappear entirely. The exudate in the corium infiltrates between the collagen bundles and may extend into the subcutaneous or submucous tissues.

Orban and Wentz (1960); These authors do not mention hydropic degeneration of the stratum germinativum. They state that large epithelial horn pearls are frequently observed in an onion-ring pattern. The formations are noted at the base of an epithelial ridge, in the centre of the epithelium, or close to its surface. These horn pearls indicate a disturbance in the normal maturation process of the epithelial cells.

Stones does not mention hydropic degeneration of the basal layer, but he states that there is atrophy of the stratum Malpighii.

Archard et al (1963); In their case report they describe a uniform band of chronic inflammatory cells, and speculate that it may represent a different stage in the course of oral lesions, or may reflect secondary involvement of the gingival tissues by contiguous inflammatory processes. The thinned atrophic epithelium may be similarly explained. They hope that, with further documentation of cases of chronic discoid L.E. exhibiting lesions of the oral mucosa, characteristic features may emerge.

As regards the staining qualities of the hyaline degeneration of the connective tissue collagen, there is disagreement. Stones, and Shafer, Hine and Levy describe a basophilic reaction, Orban and Wentz an intensely eosinophilic one, while McCarthy and Shklar state that the substance stains light pink with haematoxylin and eosin. It would be ridiculous to suggest that experienced pathologists could make a fundamental error as to the staining qualities of the connective tissue, so it must be assumed that there

is considerable variation in different cases.

Shklar and Meyer (1961), and McCarthy and Shklar report that the pa - S staining technique for mucopolysaccharides appears to be of great value in diagnosing the oral lesions of chronic lupus erythematosus. The characteristic finding is an extremely intense reaction beneath the stratum germinativum of the epithelium and around small blood vessels. These intensely staining areas represent the areas of collagen degeneration. The stratum granulosum and occasionally the stratum corneum present some reaction when stained for mucopolysaccharides, but the striking change is in the connective tissue adjacent to the epithelium. The stain is considerably more intense than that seen in cases of lichen planus in the same area. The zone of reaction is much wider, and the reaction is also noted around vascular channels.

McCarthy and Shklar feel that collagen degeneration is a constant feature in the histopathologic picture of the oral lesions of lupus erythematosus. This is supported by most of the later authors, Sugarman being the only author of note who does not include it in his findings.

(b) Acute Disseminated Lupus Erythematosus.

The histologic features of all forms of lupus erythematosus are similar, and only differ in degree, (Shafer, Hine and Levy).

Fibrinoid degeneration of connective tissue is the characteristic lesion and is seen clearly in the various internal organs, as well as in the skin and oral mucous membrane, (McCarthy and Shklar). The connective tissue ground substance becomes visible as

small clumps of eosinophilic material. The collagen fibres degenerate into amorphous eosinophilic fragments, and the degenerating ground substance and collagen fibres may be clumped together. Visceral lesions are usually seen in the endocardium and myocardium of the heart, serous membranes, glomeruli of the kidneys, and spleen. Lymphocytic infiltration occurs as a reaction to the collagen degeneration in these tissues. An interesting, possibly specific structure may be found in the lesions of visceral organs. This is termed a haematoxylin body and is probably composed of nuclear D.N.A. material.

The skin and mucosa present extensive hydropic degeneration of the stratum germinativum. Some evidence of epithelial atrophy may be present as well as spongiosis. The connective tissue of the corium presents collagen degeneration, and there is a perivascular infiltration of lymphocytic cells. Lesions of the oral mucosa are usually characterized by a greater degree of inflammatory infiltration than skin lesions. Lesions of the oral mucosa may also present non-specific ulceration in areas, rendering a microscopic diagnosis more difficult.

6. Diagnosis.

(a) Chronic Discoid Lupus Erythematosus.

All authors agree that accurate diagnosis of chronic discoid lupus erythematosus on the basis of oral mucous membrane lesions is usually very difficult. No characteristic primary lesion is present, and nonspecific tissue changes such as erosion, hyperkeratosis and erythema must be properly evaluated. The peripheral

arrangement of capillaries is often helpful, but not consistently present. As regards the histologic changes, these are often not specific enough to enable the pathologist to commit himself further than the term "compatible with". McCarthy and Shklar have recently found histochemical stains for mucopolysaccharides to be helpful in demonstrating the collagen degeneration. The presence of characteristic skin lesions is the greatest single aid in arriving at a firm diagnosis.

(b) Acute Disseminated Lupus Erythematosus.

Because of the varied symptoms, a clinical diagnosis is frequently delayed until the laboratory work is complete. The age and sex of the patient are important. Leukopenia, anaemia, and an increased blood sedimentation rate are common. Urinalysis may reveal protein and cells.

The most significant finding is the lupus erythematosus phenomenon, which is mentioned by all the later authors. The lupus erythematosus (L.E.) test, originally demonstrated by Hargraves in 1948 (mentioned by Shafer, Hine and Levy, and McCarthy and Shklar) is the single crucial test in diagnosing disseminated lupus erythematosus. McCarthy and Shklar point out that oversimplification of the original test, reliance on "weak positive" or other equivocal results, and performance by untrained personnel have to some extent weakened the true significance of the procedure. Bhaskar mentions that falsely positive reactions may occur, particularly in some cases of rheumatoid arthritis, the leukaemias, and multiple myeloma.

Shafer, Hine and Levy describe a form of the test as follows; The blood serum from the patient is added to the buffy coat of normal blood. If the patient is suffering from disseminated lupus erythematosus, L.E. cells will develop. This cell, or phenomenon, consists of a rosette of neutrophils surrounding a pale nuclear mass apparently derived from a lymphocyte. The basis of this phenomenon appears to be in the gamma globulin of the serum from the patient. McCarthy and Shklar suggest that the central cell is essentially a leucocyte which has engulfed a round mass of homogeneous nucleoprotein, that the test is positive at some time in the disseminated form, and usually, but not always, negative in the discoid form.

7. Differential Diagnosis.

(a) Chronic Discoid Lupus Erythematosus.

Lichen planus. The more classical forms of lichen planus present no problem, but in other forms differentiation may be difficult. White papules may be discerned near ulcerations, while involvement tends to be more extensive, with bilateral, often symmetrical, lesions. Histologic features may help, particularly the type of inflammatory response, and the collagen degeneration of lupus erythematosus. Typical skin lesions must be sought at times to make a firm diagnosis.

Leukoplakia. If simple hyperkeratosis is present at sites of trauma, differentiation is not difficult. However, where erosion is associated with hyperkeratosis, it is important to identify the cause of the trauma and eliminate it. In lupus erythematosus, the peripheral vascular arrangement is characteristic, and the location

may be free from mechanical irritation. Biopsy and histologic examination will usually definitely distinguish the two processes.

(b) Acute Disseminated Lupus Erythematosus.

Benign Mucous Membrane Pemphigoid. The patient with this disease would be free of constitutional symptoms, while one affected with systemic lupus erythematosus is invariably critically ill. The lack of peripheral tissue and vascular change in mucous membrane pemphigoid is significant.

Syphilis. In secondary syphilis, classically the mucous patch and split papules at the angles of the mouth are observed. Because of trauma and secondary infection, erosive lesions are sometimes seen. A serological test for syphilis should be performed if any doubt as to the nature of the disease exists.

8. Therapy.

(a) Chronic Discoid Lupus Erythematosus.

Cook stated that the eradication of infection is a valuable measure in discoid cases.

McCarthy and McCarthy state that the antimalarial drugs are very successful in controlling the chronic discoid variety.

Burket mentions the use of chloroquine, A.C.T.H., cortisone, the topical use of hydrocortisone, and the removal of focal infection as being helpful.

Stones reports that a great variety of drugs, including the intramuscular injections of bismuth and gold compounds, and other forms of treatment have been tried with varying success. Regarding

local remedies, when lotions etc. have failed, cautery by carbon dioxide snow is of value.

McCarthy and Shklar state that before the advent of the antimalarial drugs, ineffective and dangerous medications were in use. Although the skin lesions of discoid lupus respond much more quickly than the oral lesions to antimalarial drugs, satisfactory control of both is usually possible. Caution is needed in the use of antimalarials because of side effects, and these should only be used when the indication is serious. The uncommon side effects are suppression of blood-forming elements, gastro-intestinal upsets, and visional disturbances, including corneal deposits or retinal degeneration.

(b) Acute Disseminated Lupus Erythematosus.

Treatment is not in the dentist's province. Corticosteroid drugs are life sparing for various lengths of time, but most patients eventually succumb despite heroic effects. Remissions may occur that are either drug induced or spontaneous, and it is difficult to prognosticate the outcome of any individual patient. Sugarman and Stillerman (1960) report a case of systemic lupus erythematosus treated by A.C.T.H. and its allied compounds, the patient surviving for seven years to that time after being twice in the terminal state.

Moniliasis (Candidiasis).

1. Clinical manifestations,
 - (a) Thrush (oral moniliasis),
 - (b) Generalized moniliasis.
2. Aetiology - Predisposing factors.
3. Laboratory tests.
4. Histopathology.
5. Diagnosis.
6. Differential diagnosis.
7. Therapy.

1. Clinical Manifestations.

(a) Thrush (oral moniliasis).

The classical signs of the disease consist of creamy white patches often compared to "milk curds". They may occur on any area, but are most frequently observed on the tongue, palate and buccal mucosa. The white patches are moderately adherent and strip away with some difficulty, leaving a bright, erythematous base. This material represents an exudate which is almost a pure colony of the fungus. Moniliasis even in extensive cases remains on the surface of the mucous membrane and is not invasive, (McCarthy and Shklar, 1964).

There is general agreement that moniliasis is most common in young infants, in persons debilitated by age or chronic disease such as diabetes or avitaminosis, but has become considerably more common in recent years since the advent of the antibiotics.

Woodburne (1944) stated that, when moniliasis attacks the lips, it is characterized by moist symmetrical erosions at the commissures, called *perlèche*, which is almost indistinguishable from the *perlèche* of vitamin B deficiency. Lilienthal et al (1956) mention angular cheilitis as a well-defined characteristic of moniliasis. Stones (1962) gave *perlèche* as one of the oral lesions, while Kutscher et al (1964) report that *monilia albicans* is implicated in the aetiology of angular stomatitis, 4 of 33 patients having this disability. McCarthy and Shklar (1964) state that, in order to make a correct diagnosis of monilial *perlèche*, the thick white exudate must be present, and that most instances of *perlèche* are merely due to a loss of vertical dimension.

Woodburne described three forms:- An acute form in children, a rather similar subacute form in adults, and a chronic form, where the tissues are red and inflamed, particularly the tongue. Bernier (1959) treated thrush and moniliasis as two separate subjects, but this distinction is not made elsewhere in the dental literature, and does not seem warranted. Stones (1962) states that he has observed a chronic latent type in children, and that it is resistant to treatment. Lehner (1964 I) reports that, in an earlier paper in 1962, he proposed classification of moniliasis into acute and chronic varieties. Acute pseudomembranous moniliasis is the most common and may lead to acute atrophic moniliasis. He also describes a chronic hyperplastic form.

Thoma and Goldman (1960) imply that *monilia albicans* is implicated in denture sore mouth, but Burket (1961) thinks it is more

probable that the reddened, irritated mucosa beneath the dentures is related instability caused by faulty occlusion and centric relation. Kutscher et al (1964) found 22 cases of denture stomatitis out of 33 moniliasis sufferers.

(b) Generalized Moniliasis.

Hogan (1951) reported a case of moniliasis in a healthy male aged 35, with a fungus infection on the fingers of both hands which had persisted for 10 years. There was a fairly extensive lesion over the soft palate, and dysphagia.

Lilienthal, Harris and Arnott (1956) found that extra-oral lesions affect the nails, external genitalia and scalp. Despite wide destruction, the disease does not always produce changes in the general condition of the patient, although it is of considerable inconvenience, and in extreme cases, disturbingly disfiguring. Pulmonary infection resembling pneumonia has become more common in recent years, and may be fatal. In two of their cases, hyperkeratinization was most marked on hands and nails.

Meyer and Shklar (1957) report that a chronic, generalized form occurs rarely, involving the oral mucosa, nails, skin and lungs.

Shafer, Hine and Levy state that monilial infection frequently involves the skin and vagina, as well as the gastrointestinal tract, urinary tract and lungs. Thrush usually remains localized, but occasionally it extends to the pharynx or even the lungs, often with a fatal outcome.

Thoma (1963) described generalized involvement, and Reade (1964) described a fatal case in a 12-month-old aboriginal child. Long-standing involvement was present in the mouth, upper respiratory tract and probably the lungs. Cerebral irritation supervened just before death.

Lehner (1964 II) states that four clinical varieties of chronic hyperplastic candidiasis are recognized, that the intra-oral white patches may occur alone, or may be associated with distinct cutaneous lesions, or Addison's disease and hypoparathyroidism.

McCarthy and Shklar (1964) write of an extremely rare form of moniliasis with chronic generalized involvement. It is often a complication of an underlying debilitating disorder, and eventually proves fatal when manifestations occur in the lung or other vital organs. The oral lesions are extensive and may contain less exudate than in the acute forms. Cutaneous lesions are prominent, and paronychia vegetating growths are common.

2. Aetiology.

Most authors are agreed that *monilia albicans* is a normal and constant inhabitant of the mouth, Lilienthal (1955) setting the figure at 33% in the mouths of young healthy adults. McCarthy and Shklar (1964) aver that, although the organism stands out as causing the most frequent type of fungus infection of the oral mucosa, it is diagnosed far more frequently than is justified. Isolation of this organism from a diseased mucous membrane of itself means little or nothing. Even when it is observed to exist in large numbers, it

must be questioned as the main pathogen since it grows readily on many pre-existing pathologic processes. Its virulence is limited, and in all cases of oral moniliasis one should search for an underlying primary disorder which may be local or systemic. Lilienthal's tests failed to show any significant differences in virulence between strains from normal mouths and those from thrush.

Predisposing Factors; These are recounted by various authors as follows:-

Woodruff and Heseltine (1938); Babies born of mothers with vaginal moniliasis had 35 times the chance of developing thrush, when compared with infants born of noninfected mothers.

Woodburne (1944); Vitamin deficiency, possibly vitamin B complex, and chronic debilitating disease.

Lighterman (1951); Harris postulated that a long course of aureomycin therapy led to vitamin B complex deficiency, that this was restored by the administration of the vitamin, and that the aureomycin destroyed the intestinal bacteria necessary for the synthesis or utilization of vitamin B. Lighterman suggests that aureomycin destroys organisms which inhibit the growth of monilia, increasing the virulence of the fungus, and also the tissues are more susceptible to infection by reason of the vitamin B deficiency.

Woods and Manning (1951) reported 25 cases of clinical moniliasis following the clinical use of penicillin, aureomycin and chloramphenicol. In vitro studies of four strains of monilia showed that these antibiotics have no stimulating or suppressing effect on the rate of growth. Suppression of the bacteria flora coexisting

with monilia and competing for nutrition in the same substrate was thought to be the most probable cause for monilial overgrowth and host infection. Their clinical observations did not permit conclusions regarding the importance of changes in vitamin biosynthesis or other physiopathological reactions lowering host resistance to monilial invasion.

Simpson (1951) reported two cases where there was a possible link between trauma and onset of the lesions. In both cases the patients were wearing full dentures, and a slightly atypical lesion in the cheek along the line of the occlusal plane was evident.

Lilienthal; An important role is played by the tissues or the immunity mechanisms and/or microbial population in the mouth. Diabetes and phthisis can lower the resistance to infection, and antibiotics can radically alter the microbial balance, enabling fungus overgrowth.

Carpenter (1955); Data indicate an increase in the numbers of yeast-like fungi since the advent of antibiotic therapy. There was no demonstrable change in the frequency of the species.

Trott (1955); presented a case in a healthy male, aged 22, who had penicillin treatment for two attacks of Vincent's infection in seven weeks, and who had been treated intermittently with antibiotics over a period of 18 months. The penicillin did not cause the monilia to flourish, in fact the clinical signs disappeared without treatment.

Lilienthal, Harris and Arnott (1956); Topical use of antibiotics, or prolonged dosage intramuscularly may disturb the equilibrium of the oral flora. Bratland and Holten suggest that treatment with corticotropin and cortisone may induce severe monilial of the oral cavity, pharynx, larynx and lungs.

Enhancement of the pathogenicity of monilia by aureomycin alone is further augmented by cortisone in mice. Further experimental investigations with mice have indicated also antagonism between cortisone and other hormones with respect to the pathogenesis of the disease.

The possibility that hyperkeratinization plays some part in the aetiology and persistence of the disease cannot be entirely overlooked. Two patients of this report showed marked hyperkeratinization on the hands and nails.

Meyer and Shklar (1957); Affects infants or adults debilitated with chronic disease or on sustained antibiotic therapy.

Smith (1959); Most common in infants and patients with wasting diseases. Ill-fitting dentures predispose to the condition in the mouth.

Kozinn et al (1959) found no increase in the incidence of thrush among infants in the immediate vicinity of "infected" infants. The danger of air-borne transmission or infection by the nursing personnel appeared to be negligible, and isolation of infants with oral thrush did not diminish the incidence of this disease during the first two years of life.

Bernier (1959); *Candida albicans* is likely to take part in a mixed infection, and then the clinical features are quite indistinct. The presence of prosthetic appliances seems to contribute to the retention of the monilia, which actually enters into the fabricating material, so that lesions are often seen in adults, whereas thrush is essentially a disease of debilitated infants. Instead of the classical "furring" seen in thrush, these infections tend to mimic those caused by bacteria. Allergy may enter the picture.

Burket (1961); Broad-spectrum antibiotics alter the oral bacterial flora and stimulate the yeast forms. Formerly chiefly in premature, debilitated or malnourished children. Hormonal imbalance and radiation therapy may predispose to moniliasis.

Stones (1962); Thrush is seen in infants. Ludlam and Henderson found a higher incidence in bottle-fed babies, and in overcrowded nurseries and hospitals. Organisms were found in one-third of nurses without lesions, and in pooled breast milk. Infection from a vaginal moniliasis during birth is mentioned.

It occurs in adults following debilitating diseases. The organism is found in unclean mouths and under dirty dentures. The effect of aureomycin and cortisone is mentioned.

Shafer, Hine and Levy; Infection of newborn babies, the effect of antibiotics are described, and the predisposing effect of chronic disease.

Thoma (1963); Infection in poorly nourished infants, infection from vaginal moniliasis of the child, debilitating diseases

are considered. Local causes mentioned are a decrease in the pH of the mouth, inadequate saliva secretion, and contaminated dentures. Riboflavin deficiency predisposes to moniliasis, as do the antibiotics.

Kutscher et al (1964); In 33 patients, the aetiology in 21 was related to denture stomatitis, in 4 to angular stomatitis, in 5 no aetiological factor was seen, and in 3 there was an antibiotic induced stomatitis.

Lehner (1964 I); In the debilitated patient, infection may be endogenous from the gastro-intestinal tract, or exogenous as a result of contact with carriers, contaminated objects or patients with moniliasis. Thrush in infants is due to direct contact with vaginal moniliasis during parturition. The role of antibiotics, corticosteroids and cytotoxic drugs as promoting agents is confirmed.

McCarthy and Shklar (1964); One may find many monilial organisms in the normal mouth or in other disease processes. This is especially true in association with broad-spectrum antibiotic therapy. Their presence without the milky-white exudate is meaningless. True moniliasis is an uncommon complication of antibiotic therapy. When thrush occurs, some underlying predisposing factor is usually present. Sick, poorly developed infants and debilitated elderly persons represent the most commonly afflicted groups. Also it may be seen among patients with poorly controlled diabetes, pregnant females, and patients receiving corticosteroid and broad-spectrum antibiotic therapy to a greater degree than in otherwise "normal persons". The few patients they have encountered

have been principally those with an advanced malignant growth, and infants.

3. Laboratory tests.

Meyer and Shklar suggest that examination of the surface film by means of a smear stained with gentian violet or methylene blue will disclose the spores and mycelia of the monilial organism.

Burket recommends that scrapings be treated with a 10% potassium hydroxide solution and studied in a hanging drop preparation. These will reveal the typical clusters of spores and intertwining hyphae. Cultural studies using Sabouraud's or corn-meal agar will also aid diagnosis.

Stones also states that scrapings yield on smear examination or culture one of the saccharomycetes, the usual type being the *Candida albicans*.

Shafer, Hine and Levy describe the technique as follows:-
Fragments of the plaque material may be smeared on a microscopic slide, macerated with 20% potassium hydroxide, and examined for the typical hyphae. Organisms may also be cultured on a variety of media.

Colonies of *Candida* are enamel white, and have a peculiar odour because of fermentation of sugars, (McCarthy and Shklar).
The genus *Candida* differs from the true yeast in that it produces hyphae as well as budding cells. Since *Candida albicans* is the only regularly pathogenic yeast, it is important to recognize its important diagnostic features:-

1. Characteristic chlamydospores are produced on corn-meal agar.

2. Spherical clusters of budding cells are produced at the hyphae nodes.
3. Intravenous inoculation into a rabbit kills the animal in four days, producing multiple abscesses in the kidney.

4. Histopathology.

Meyer and Shklar describe the histologic findings as destruction of the epithelium and invasion of mycelia into the underlying tissue.

Bernier states that the histologic picture is not specific. There is denudation of the superficial epithelium, and before sloughing, it shows marked oedema in the upper layers. Intermingled with fibrin, leucocytes and desquamated cells are the organisms. There are many other inhabitants whose influence in the primary reaction is open to question. A diffuse, chronic inflammatory reaction in the upper corium is fairly characteristic, being perivascular. In older lesions, scarring occurs with a diminution in the blood supply and a gradual disappearance of the cellular infiltrate.

Orban and Wentz; The creamy, curdy lesions are due to the fungus growth, abscess formation and necrosis in the epithelium, in which large spaces develop and then become filled with leucocytes. These abscesses frequently burst into the oral cavity. The cellular debris in the vacuolated areas enlarges and finally leads to complete necrosis. In the subepithelial connective tissue polymorphs dominate the field, migrating from dilated capillaries. Much of the connective tissue is necrotic.

Lehner (1964 I); That the mycelial phase of monilia is the invasive form was confirmed by the presence of sections of monilial lesions where the constant pattern seen in 20 cases was the presence of yeast cells superficially and proliferating pseudohyphae deep in the tissue.

Lehner (1964 II); Histologic examination of 23 cases showed a variety of mucosal changes; (a) Candidial invasion of keratin, parakeratin or stratum spinosum, forming a fungal plaque, consisting of fungus, necrotic epithelium, fibrin, bacteria and mucin. Often there was no host reaction; (b) Plaque formation may be associated with oedema and micro-abscesses in the stratum spinosum, with a mild leukocyte reaction in the corium, (c) with mucosal ulceration, masses of mycelia may invade the corium and thrombosed blood vessels, (d) numerous layers of desquamated epithelium infiltrated with fungal hyphae may accumulate over uninvolved mucosa, (e) shedding of fungal plaque may carry with it layers of epithelium, giving rise to acute atrophic Candidiasis. Histologic examination of chronic hyperplastic candidiasis shows keratosis, parakeratosis, acanthosis or pseudo-epithelial hyperplasia and a dense chronic inflammatory cell infiltrate in the corium. The stratum corneum and spinosum are invaded by hyphae of Candida, under which oedema and micro-abscesses may be found.

Cawson (1964); Biopsy of inflammatory lesions of oral mucosa (15 cases) due to monilia indicated the importance of the mycelial phase. The histologic appearances were characteristic. Invasion of the epithelium was into the superficial layers by

mycelium only, usually oriented at right angles to the surface. There was an inflammatory response with striking intraepithelial oedema and formation of superficial micro-abscesses, together with loosening and shedding of the superficial epithelium and mycelium. More deeply, there was epithelial hyperplasia and a chronic inflammatory reaction in the corium. The histologic changes indicate that the mycelium is the form by which *Candida* invade the tissues and that the mycelium should be looked for in direct smears.

5. Diagnosis.

Meyer and Shklar state that the diagnosis is made from the clinical appearance, examination of the smear, and cultivation of the fungus on Sabouraud's medium.

Glickman (1958) finds that the diagnosis is based on the history, clinical appearance of the lesions, microscopic study of smears, and cultural studies.

Burket is of the opinion that a definite diagnosis can be made by study of scrapings in a hanging drop preparation, and by cultural studies, while Stones also uses smears and cultures for diagnoses.

Shafer, Hine and Levy state that there must be actual penetration of the tissues, and recommend smears and cultures for diagnoses.

Lehner (1964 I) finds that a direct smear may assist in differentiating the saprophyte which is found in the yeast phase, from the pathogen found in the mycelial phase. Twenty smears

were examined from patients without signs of moniliasis but in whom monilia was cultured from saliva, and none of these demonstrated the mycelial phase.

Cawson (1964) also confirms that the mycelium should be looked for in direct smears.

McCarthy and Shklar (1964) suggest the following criteria for making a diagnosis of moniliasis;

1. The presence of numerous budding cells and filaments in the smear from the suspected lesion.
2. A positive culture of the material.
3. Typical creamy patches on the oral mucosa.
4. Elimination of other diagnostic possibilities.

6. Differential Diagnosis.

Woodburne pointed out the need to differentiate moniliasis from herpes, syphilis, erythema multiforme, discoid lupus erythematosus, lichen planus, and leukoplakia.

Burket thinks thrush should be considered as a diagnostic possibility if the patient complains of a sore mouth or throat, with or without perleche, following antibiotic therapy. Constitutional symptoms are mild compared to streptococcal stomatitis and pharyngitis or diphtheria. Chronic irritation under dentures should only be diagnosed as moniliasis if supported by cultural studies. The history of its development and the possible associated medication will assist in differentiating moniliasis from leukoplakia and lichen planus. In thrush, the tissues have a macerated appearance, are flexible, and the lesions can be removed with firm pressure, leaving

a painful, bleeding surface. This is not possible with lesions of oral leukoplakia. Smears and cultures are conclusive.

Lehner (1964 I) points out that chronic hyperplastic candidiasis may be very similar to leukoplakia, but lichen planus and white sponge naevus have many distinguishing features. He states that the histopathology of the chronic hyperplastic form is specific.

McCarthy and Shklar state that any disease capable of producing a white patch must be considered. Leukoplakia and lichen planus can be dismissed readily since they produce a fixed tissue reaction that cannot be scraped from the surface of the oral mucosa as the exudate of thrush. Mucous patches, aspirin burn, and any exudative process may suggest moniliasis. Laboratory study will reveal the true nature of the exudate.

7. Therapy.

Methods of treatment described are as follows:-

Woodburne; Correct the underlying condition; improve oral hygiene. For acute thrush - 1% aqueous solution of gentian violet may be used; while for chronic cases, 1-5% aqueous solution or tincture of gentian violet may be used. Lugol's iodine is helpful, silver nitrate, potassium permanganate, thymol, and X-ray therapy have been used. Coagulation, cautery, fulguration are condemned.

Lighterman; Moniliasis responds readily to frequent

rinsing with an alkaline solution, the application of gentian violet 1:10,000, and the administration of vitamin B complex. Administration of vitamin B is recommended with aureomycin therapy.

Woods and Manning: The use of vitamin B complex with antibiotics seems to have some value.

Lilienthal (1955) found the application of 1:1,000 aqueous solution of merthiolate was effective.

Meyer and Shklar; The application of 1% solution of gentian violet several times daily brings an improvement in 4-5 days.

Smith (1959); The application of 1:10,000 gentian violet may be carried out. For severe infection in children, amphotericin B should be tried.

Bernier; The application of aniline dyes is of great value, the reaction usually receding in a few days. Where monilia is involved with denture stomatitis, the denture should be remade.

Orban and Wentz; Local therapy; (1) the application of 20% aqueous solution of sodium caprylate, locally and as a mouth rinse, (2) the application of 1% gentian violet to the lesions 2-3 times daily, (3) the topical application of mycostatin, 100,000 units, 3-5 times daily, (4) X-ray and ultraviolet radiation, (5) Lactinex (mixed bacillus) tablets. Systemic therapy; (1) a high vitamin diet, (2) potassium iodide by mouth.

Thoma and Goldman (1960); Local therapy consists in painting the affected areas with Scott's solution, gentian violet, iodine, chromic acid, 1% methylrosaniline chloride,

1% formaldehyde. Systemic therapy - mycostatin, 500,000 units three times daily gives good results.

Burket; Patients on antibiotic therapy should receive vitamin B complex therapy and possibly buttermilk. Oral moniliasis may be treated with a 20% aqueous solution of sodium caprylate, and a suspension containing 100,000 units/ml. of mycostatin has been found effective. All antibiotic and corticosteroid therapy should be stopped. The effectiveness of boric acid solutions and crystal violet leave much to be desired.

Stones; 1% Gentian violet, 10% sodium caprylate are effective. Nystatin in a suspension containing 100,000 units/ml. is also used. Improve oral hygiene; prescribe an antiseptic mouth-wash.

Shafer, Hine and Levy; New antifungal agents such as nystatin have been beneficial. Suspensions of nystatin, held in contact with the oral lesion, have been successfully used, even in chronic, severe cases.

Kutscher et al (1964); Amphotericin B had a marked suppressant or curative effect on all lesions. In denture stomatitis the effect was suppressive, recurring after withdrawal. In angular stomatitis, there was marked improvement in 3, slight improvement in 1, occurring in one week. In 5 cases of oral moniliasis, there was complete disappearance in 4, moderate improvement in 1 case. There were recurrences in 2, and these responded to reinstitution of therapy. In antibiotic-induced stomatitis, there was complete disappearance in all 3 cases. There were no side-effects.

Lehner (1964 I); Nystatin is useful. Failures in this series were probably due to inadequate concentration of nystatin at the site of the lesion. Nystatin is poorly absorbed from the gastro-intestinal tract, so continuous high local concentration is achieved only by keeping tablets in the mouth, and not swallowing them. No complications were observed from treatment with 500,000 units daily for 9 months.

McCarthy and Shklar; (1) Correction of underlying predisposing conditions by correcting nutritional deficiencies, controlling diabetes, and strengthening the general resistance; (2) application of topical antimonilial medications. Nystatin and amphotericin are two reasonably potent antimonilial drugs. Other suitable medications are Naprylate and Chlordantoin. Gentian violet is painted on a variety of stomatitides, thus effectively concealing the underlying pathologic changes. It is effective in moniliasis, but it should be used in a 0.5% aqueous solution, as higher concentration may produce local reactions. Because of its colour, they prefer the preparations mentioned.

Geotrichosis.

This is a fungal disease similar to moniliasis in its clinical features, but caused by organisms of the Geotrichum species. Smith (1959) and Shafer, Hine and Levy are the only authors found who mention this disease.

Clinical Features.

The most common lesions are those of the lungs and oral mucosa, although cutaneous and intestinal tract lesions occur on occasions. The lung involvement produces symptoms of pneumonitis or bronchitis, but organisms can be detected in the sputum.

Oral Manifestations.

These are identical with those of moniliāsis. The differentiation is made only by microscopic examination and/or culture of the organisms.

It is seen frequently in debilitated persons, or as a secondary type of infection in patients.

Histologic Features.

The organisms are small, rectangular-shaped spores measuring approximately 4 X 8 microns, often with rounded ends. The tissue reaction is a nonspecific, acute inflammatory one.

Treatment.

Treatment is nonspecific, there being insufficient data on the effects on geotrichosis of the drugs used in treating moniliasis.

Benign Migratory Glossitis.

Synonyms used are; Geographic Tongue; Wandering Rash of the Tongue; Glossitis Areata Exfoliativa; Erythema Migrans.

Benign migratory glossitis will be described under the following headings:-

1. Occurrence,
2. Aetiology,
3. Clinical features,
4. Histopathology,
5. Therapy.

1. Occurrence.

The following incidence Table was presented by

Meskin et al (1963):-

Study	Type of Sample	Sex	Number Examined	Number Affected	%
McCarthy (1941)	All ages, referred for skin disorders.	mixed male & female	2,301	55	2.40
Halperin et al (1953)	Dental Clinic patients, all ages.	male	1,199	13	1.08
		female	1,279	21	1.64
		total	2,478	34	1.37
	Subgroup, ages 10-30 years.	mixed	1,388	18	1.30
Rahaminoff & Muhsam (1957)	Children of Jewish Refugees in Israel, ages 0-2 years. Repeated observations.	male	2,886	453	15.70
		female	2,539	322	12.70
		total	5,245	755	14.40
Meskin et al (1963)	University Students; Caucasian, ages 17-21	male	1,409	16	1.14
		female	2,259	26	1.15
		total	3,668	42	1.15

Prinz and Greenbaum (1939) stated that the ages from 1 to 5 are especially favourable to its appearance, but that it is found frequently in women of all ages, and occasionally in men. The ratio of women to men was placed at 5:3.

Halperin et al did not confirm Prinz and Greenbaum's suggestion that benign migratory glossitis is more frequently observed from 1 to 5 years of age.

Cheraskin and Langley (1956) commented that the disease is common in highly emotional women.

Sharp et al (1956) stated that over 25% of geographic tongues are associated with the fissured tongue, in which the filiform papillae are of an abnormal anatomic pattern.

Cooke (1962) studied 39 cases of the disease, 20 of whom were females, 19 were males, and found that 14 were in the fourth decade, 6 in the third decade, 6 in the fifth decade, 6 in the sixth decade, one in a child of 4.

McCarthy and Shklar (1964) found that almost 50% of their patients also have presented a fissured tongue.

2. Aetiology.

All authors are agreed that the aetiology is either completely unknown or obscure. However, various theories are mentioned, or comments made:-

Halperin et al state that the clinical history of benign migratory glossitis is similar to that of neurodermatosis and a psychosomatic background should be considered.

Sharp et al; A relationship to dietary and digestive function and to bacterial floral variations within the gastrointestinal tract is suggested.

Prinz and Greenbaum; Half of the recorded cases have a rachitic history.

Cheraskin and Langley; Three theories mentioned are the link with rickets, a neuropathic basis, and allergy.

Bernier (1959); The possibility of congenital disturbance should be considered, particularly in view of the many abnormalities which affect the tongue, and the persistence of the reaction.

Cooke (1955); Referred to the frequent association with fissured tongue, and considered that the disease may be due to irritation from organisms harboured in the fissures.

Orban and Wentz (1960); Women of nervous temperament during the menstrual period may present the lesions. Children and persons prone to allergic reactions may have a predisposition.

Cooke (1962); The sufferers from benign migratory glossitis are often of anxious temperament.

Shafer, Hine and Levy; A psychosomatic background has been suggested.

3. Clinical Features.

Descriptions given by various authors do not differ in any important features. A representative one is that of Colby, Kerr and Robinson (1961):

There are migrating circinate or ovoid inflammatory lesions on the dorsum of the tongue. (Cooke, 1955, reported lesions on the

palatal and labial mucosa, Cheraskin and Langley, on the lips, sublingual space and soft palate, McCarthy and Shklar, on the ventral surface of the tongue, and other areas of the mouth.) These lesions, which arise without apparent cause, are red and slightly depressed, and have a greyish-yellow border. The redness is related to loss of the filiform papillae, desquamation of the superficial prickle cells, and hyperaemia. Careful examination will usually reveal that there is some regeneration of filiform papillae centrally and that the redness is more intense near the periphery. Patients may complain of a slight burning sensation, but usually the lesions are painless. (Sharp et al state that 60% of patients complain intermittently of soreness and rawness of the affected areas, while 30% complain of varying sensations of generalized burning of the tongue). The degree of migration varies with the case. There may be periods when the tongue is completely healed. This disease may persist for years.

4. Histopathology.

Thoma and Goldman describe the histopathology as follows:-

The white lines at the periphery of the lesions are caused by thickening of the filiform papillae and hypertrophy of the epithelium (parakeratosis). The epithelium shows some hyperplasia, oedema, and varying degrees of keratosis, particularly at the border of the patches. The epithelial rete pegs may be pronounced and blunted at the end, while in between these extensions, the epithelium may be thinned out, in which instance, exfoliation is noted clinically.

(Bernier draws attention to the similarity of the microscopic picture to that of psoriasis). A rather dense, inflammatory exudate (lymphocytes, plasma cells and some polymorphs) may be seen subepithelially.

5. Therapy.

McCarthy and McCarthy (1958) pointed out the need to differentiate benign migratory glossitis from mucous patches of syphilis.

Treatment is generally unsatisfactory. As the condition is benign, only reassurance is necessary. To ease discomfort, topical anaesthetics and the avoidance of spicy foods have been recommended.

Hairy Tongue.

Clinical Features.

Hairy tongue is a condition characterized by gross elongation of the filiform papillae of the dorsum of the tongue which results in a dense, tangled feltwork of papillae superficially resembling hair. The individual papillae, with their keratin extensions, trap food debris and provide a harbour for growth of bacteria and fungi. The colour of the affected tongue varies from yellow to black, depending on the relative amounts of keratin, the types of micro-organisms present and the extrinsic staining. Although hairy tongue is usually asymptomatic, persons with this condition may complain of gagging, nausea, bad taste, and halitosis, (Standish and Moorman, 1964).

Bhaskar (1961) describes white hairy tongue and states that some cases may show brown or black discolouration of the "hair", usually due to some exogenous pigment in foods and medicines. Smith (1962) describes the colour as white to yellow or brown to black, being related to staining factors such as foods, antibiotics, tobacco and micro-organisms.

Bhaskar (1963) states that white hairy tongue is usually asymptomatic, but food impaction may lead to inflammation and pain (glossodynia).

Shafer, Hine and Levy (1963) describe the colour of hairy tongue as being yellowish-white to brown or even black, depending on staining by such extrinsic factors as tobacco, certain foods, medicines or chromogenic organisms of the oral cavity.

McCarthy and Shklar (1964) title their description of this condition Lingua Nigra (Black Hairy Tongue), and state that it must be divided into two groups:-

1. True lingua nigra which manifests not only hyperpigmentation but also elongation of the filiform papillae.
2. Pseudo lingua nigra which shows merely a black discolouration without the associated papillary hyperplasia.

True cases of lingua nigra are rare, although they have observed some increase in the past two or three years. Previously, the majority of patients were elderly men with poor oral hygiene and who were heavy smokers. Recently they have seen this condition in a number of young females with clean mouths who were non-smokers and had not been taking any medication. The process involves the mid-portion of the tongue. Some patients fail to show any of the marked pigmentary changes when the papillae are lengthened, and a few may present merely a yellowish-brown colour.

Aetiology.

Bhaskar (1961) states that, although fungus growth and an allergic basis have been suggested as the cause of white hairy tongue, it is as yet of unknown aetiology.

Smith describes the suggested possible causes as anti-biotics (e.g., penicillin and streptomycin), certain fungi and poor oral hygiene, also metabolic disease, gastro-intestinal disorders, and blood dyscrasias. It is possible, however, that the hairy tongue is simply a coincidental finding associated with several systemic diseases. In the case of long-term use of antibiotics, it

has been suggested that there is suppression of growth of the normal oral flora, and resulting overgrowth of fungi.

Bhaskar (1963) states that the elongation of the filiform papillae is due to the accumulation of keratin. White hairy tongue is the result of dehydration, or the cause may be undemonstrable.

Shafer, Hine and Levy comment that, although it is true that many different organisms, including *Candida albicans*, may be cultured from scrapings of the papillae, there is no proof of a cause-and-effect relation. There is no clear evidence supporting the causative effect of systemic disturbances, drugs or antibiotics, or the effect of smoking. Hairy tongue is rather frequently seen in patients who have had extensive X-ray radiation about the head and neck for treatment of a tumour. It is nearly always found that radiation was directed through some or all of the salivary glands, thereby undoubtedly altering the function to some extent. The ensuing hairy tongue is probably due to some change in the local oral environment, although it is not known whether this is a physical or chemical change in the saliva itself, or a change in the microbial flora.

Standish and Moorman state that the cause of hairy tongue is obscure, but has been related to antibiotic therapy, chemical oral irritants such as smoking or oxidizing mouth washes, and to irradiation therapy. Fungi have been cultured, but are considered to be simply saprophytes.

McCarthy and Shklar state that, when only the dark discolouration is present, antibiotic therapy is responsible. The mechanism for papillary change is not known. It would be logical to explain this process as the result of chronic irritation as in the hyperkeratinization of leukoplakia. Since the elongation of the papillae is essentially a similar pathologic change, one might expect the same aetiological factors operating for both. Only saprophytic bacteria and fungi have been isolated from scrapings.

Histologic Features.

According to various authors, the picture is as follows:-

Orban and Wentz (1960); There are hyperkeratinized, hyperplastic filiform papillae. The base of the filiform papillae is widened. The connective tissue is oedematous, and its projections into the epithelium appear clublike. A moderate inflammatory reaction is present immediately below the epithelium.

Bhaskar (1961); There is hyperplasia of the filiform papillae but the epithelial cells are all normal. The connective tissue may show plasma cell and lymphocytic infiltration.

McCarthy and Shklar; There is a nonspecific picture of chronic inflammation with extensive elongation and overgrowth of the papillae. Masses of bacterial and mycotic micro-organisms are observed between hyperplastic papillae.

Standish and Moorman; There are elongated papillae with tangled masses of keratin appearing as extensions of individual papillae and enmeshing numerous bacterial colonies and amorphous debris. The total thickness of the epithelium is not increased otherwise, and

the rete pegs are of the usual pattern. Mitotic activity is not prominent and there is orderly maturation of cells. The upper spinous layer of cells demonstrates pyknotic nuclei and "ballooning degeneration" or clear spaces in the cytoplasm.

Treatment.

Various authors recommend the following treatment:-

Cheraskin and Langley (1956); Establish good oral hygiene.

Drugs being used should be discontinued. Use the toothbrush on the tongue. Swab with 10-15% salicylic acid; 3% hydrogen peroxide removes the discolouration; 20% sodium caprylate may be applied as a fungicide.

Orban and Wentz; Improve oral hygiene. Apply 20% sodium caprylate. Lactinex tablets consisting of a mixed culture of bacillus acidophilus and B. bulgaricus can be used to restore the normal bacterial flora. Eliminate possible aetiologic factors.

Bhaskar (1961); No treatment is needed. Daily brushing or gentle scraping is helpful.

Smith; Triamcinolone acetonide brings improvement and is the treatment of choice.

Weinstein and Rosencrans (1962); An ointment of triamcinolone acetonide was used with the thought in mind that the well-known antimitotic and anti-inflammatory activity of the glucocorticoids might arrest the process. Treatment of this case was successful in two days after failure with all other treatment for five weeks.

Shafer, Hine and Levy; The tongue may be brushed to promote desquamation and remove the debris.

McCarthy and Shklar; Brushing, scraping and shaving of the papillae may reduce the length so that the patient is asymptomatic. Keratolytic solutions such as 5 to 10% salicylic acid in alcohol may be applied carefully and washed away after a few moments of contact.

Standish and Moorman; Podophyllin resin was used successfully in the treatment of hairy tongue in 35 cases. Response to treatment was slower when podophyllin in mineral oil was used, than when the vehicle was equal parts of acetone and alcohol. The changes were believed to be a result of maturation changes (mitotic arrest) in the deeper portions of the epithelium, rather than a direct keratolytic effect. Because of its cathartic properties, none of the preparation should be swallowed, and excess should be swabbed from the tongue. Care should be taken to protect the eyes from the material.

Fordyce's Granules.

(Fordyce's Spots or Disease)

Fordyce (1896, quoted by Halperin et al, 1953) first described these spots and suggested that they were the result of degeneration. It was later shown that the spots are due to ectopic sebaceous glands.

Occurrence.

White reported that for every three cases of Fordyce spots that occur in women, only two occur in men, while the ages 20 to 40 show the greatest number of cases. Margolies and Weidman studied 248 individuals, found men and women equally affected, and 70% of the group had spots, (Halperin et al).

In Halperin et al's study, 82% of 2,478 patients showed Fordyce spots. Although only 59% children under 11 had spots, each succeeding decade showed them in 83-88% of those examined.

Miles (1958) found a substantial increase related to puberty, with a further increase during adult life.

Aetiology.

All authors are agreed that the spots are sebaceous glands similar to those in the skin associated with hair follicles. Burket (1961) suggests that the hypertrophy of the aberrant sebaceous glands is probably the result of the trauma of chewing, irritation from smoking, bacteria, or a combination of these factors.

Clinical features.

Halperin et al found the buccal mucosa the most common site, 71% of all patients having them there, compared to 53% in the

retromolar region, 49% in the lip. The greatest sex difference was in the labial region, where males showed 52% occurrence, females 45%. Miles found that the lower lip and the zone of mucosa close to the muco-cutaneous junction of the upper lip were almost invariably devoid of them.

Bernier (1959) described the spots as tannish-white, Burket, yellow, Stones (1962), yellowish, Shafer, Hine and Levy (1963), yellow, McCarthy and Shklar (1964), white-yellow.

The spots are either discrete or plaques, often slightly raised, usually in a bilaterally symmetrical pattern on the mucosa of the cheeks opposite the molars, also on the inner surface of the lips and in the retromolar region lateral to the anterior faucial pillars, (Shafer, Hine and Levy). Occasionally on examination with a hand lens, a minute orifice from the gland duct may be observed, (Stones).

Microscopic Features.

The spots are identical with the sebaceous glands normally seen in skin, but are not associated with hair follicles. There may be a few or a great many lobules, all around one or more ducts which open on the surface of the mucosa. These ducts may show keratin plugging.

Treatment.

The glands are innocuous, have no clinical or functional significance and require no treatment.

Familial White Folded Dysplasia of Mucous Membrane.

This condition will be reviewed under the following headings:-

1. History and nomenclature.
2. Clinical manifestations.
3. Histopathology.
4. Diagnosis.

1. History and Nomenclature.

Trott (1956) quoted Burns (1915) who described generalized keratoderma in a boy aged 16 where there was involvement of the ears, eyes, nasal and buccal mucous membranes. In the buccal and nasal mucosa there was superficial thickening of the epithelium which closely resembled the clinical picture of leukoplakia. Biopsies taken from the right forearm and back of the neck showed a general thickening of the stratum corneum. In many areas there was a direct transformation from basal to horny layer, whilst in the corium there was no inflammatory infiltration.

Numerous authors quote Cannon (1935) as first describing this condition. He reported a case of "white sponge naevus of the mucosa" in a woman aged 38. The epithelium of the cheeks, the side of the tongue, palate, gingiva, and floor of the mouth was thickened and showed a peculiar white tint. A similar type of lesion existed on the labia, vagina, upper part of the anal canal and rectum. There was a family history of "white mouth", in the patient's son, two sisters, a brother, mother, and a maternal aunt. The appearance

was similar to leukoplakia, but the gingiva showed numerous follicular openings over a greyish-white surface. Biopsy revealed hyperkeratosis.

The term "white sponge naevus" is also used by Bernier (1959), Thoma and Goldman (1960), Colby et al (1961), Smith (1962) and McCarthy and Shklar (1964).

Ludy and Shirazy (1941, quoted by several authors), reported a similar case and termed it "congenital leukokeratosis". Other names used are as follows:-

Everett and Noyes (1953) - White folded gingivostomatitis,
also used by Burket (1961).

Trott - Congenital keratosis.

Kinney and Darifield (1956) - Pachyderma oralis.

Cooke (1956) - Oral epithelial naevus.

Zegarelli and Kutscher (1957) - Familial white folded
hypertrophy of mucous membranes.

Darling and Fletcher (1958) - Familial white folded
gingivo-stomatitis.

Zegarelli et al (1961) - Familial white folded dysplasia
of mucous membranes (also used by Shafer, Hine and
Levy, 1963).

Stones (1962) - Developmental leukokeratosis.

To this reviewer, familial white folded dysplasia (or
hypertrophy) of mucous membrane seems the most appropriate term.

2. Clinical Manifestations.

Bernier feels that the suggestion that the reaction is congenital is not acceptable, as the association is most likely fortuitous.

The clinical features are described quite uniformly in the literature. The condition is congenital in many instances. In other cases it does not appear until infancy, childhood or even adolescence, by which time it reaches its full severity. It appears to follow a heredity pattern as an autosomal dominant trait.

The lesions may be widespread, involving the cheeks, palate, gingiva, floor of the mouth and portions of the tongue. The mucosa appears thickened, folded or corrugated, with a spongy texture and a peculiar white opalescent hue. Sometimes the folding is minimal. The lesions are nearly always symptomatic. Occasional cases are reported with lesions of other mucosal surfaces, including the vagina and labia, anus, rectum and nasal cavity.

Everett and Noyes found, on the gingiva of one patient with this condition, vesiculation and desquamation.

Trott's case, a single woman of 28, showed three gingival lesions in the molar areas. (This case must be considered atypical, if within this category at all - Reviewer).

Smith comments that most investigators state that no treatment is necessary, but this is not always true. If there is chronic irritation, the lesion should be treated just as any other area where chronic irritation is a factor in epithelial changes.

If there is a possibility of epithelial change, surgical removal should be considered. If the area is extensive, a skin graft would be needed.

3. Histopathology.

Histologic features described by various authors are as follows:-

Trott; Marked hyperkeratosis but no acanthosis was seen. There were chronic inflammatory cells seen some distance from the basal layer of the epithelium.

Kinney and Darifield; There was hyperplasia of the epithelium, pronounced parakeratosis, the cells were large in the Malpighian layer, and contained granules of coarse hyalin material. Lymphocytes were present in the connective tissue.

Cooke; There was hyperplasia of the prickle cells. There were two main histologic appearances; there was either an increased rate in the production of keratin, giving the keratin layer a definite basket weave pattern, or there was failure of the keratin to separate. The underlying corium was normal. A peculiar dyskeratosis below the granular layer could be seen, that would appear to impair the mechanical properties of the epithelial layer, so that it split, exposing the underlying corium.

Darling and Fletcher; The epithelial pegs were swollen and distorted, the lower rete border being well marked and intact. There was considerable parakeratosis, the superficial squamæ having a "shaggy" appearance due to fragmentation. This was thought to be due to defective maturation caused by the marked hydropic degeneration

of the deeper cells. There was a mild degree of lymphocytic inflammation in the papillary corium, but no inflammatory change was found in the deeper submucosa.

Burket; There is marked thickening of the epithelium associated with hyperplasia, and at times, vacuolization of the epithelial layers. The lesion is caused by a thickening of the normally ordered layers of the epithelium.

Colby et al; The histologic findings are distinctive and diagnostic. The epithelium is quite hyperplastic, and the rete pegs are broad and fused. Parakeratin is present in varying amounts on the surface, and in some regions, extends deeply into the Malpighian layer. A marked oedema, both intra- and extra-cellular, is evident in the prickle-cell layer. Small vesicles are occasionally formed. Many of the prickle cells that are not vacuolized are keratinized. These cells, which are very distinctive, appear as discrete, circular, red bodies with blue-staining centres.

Zegarelli et al; There is a thickening of all layers of the epithelium (up to 45-50 cells in thickness). The zonal layering is essentially normal, marked acanthosis is also frequent. Many cells show marked swelling and vacuolization (containing glycogen in at least one of the biopsies studied) in the granular and prickle-cell layers. Many mitoses in the basal and prickle-cell layers were seen in one biopsy specimen, and somewhat fewer mitoses were noted in two additional sections. Characteristically,

the epithelial cells, together with their arrangement and form, have an entirely benign appearance.

Smith; The changes are acanthosis, and spongiosis. There is a rather typical pattern of elongation and fusion of the rete ridges, parakeratosis, and a striking change is the failure of the epithelial cells, especially in the outermost layers, to stain adequately, causing a washed out appearance. There may be oedema and varying numbers of chronic inflammatory cells in the connective tissue area.

Stones; There is marked thickening of the epithelium, largely due to parakeratosis or hyperkeratosis. The underlying corium is normal and little or no inflammation is seen.

Shafer, Hine and Levy; The histologic features are characteristic, but not pathognomonic. They are thickened epithelium, intact basal layer, intracellular oedema in the entire spinous layer, (the spinous cells showing pyknotic nuclei), and possibly mild inflammatory cell infiltration in the submucosa.

It seems significant that until 1958 there was little distinctive in the histologic findings of this condition, but since Darling and Fletcher's report, all writers except Stones emphasize oedema of the Malpighian layer. Colby et al's assertion that the microscopic picture is distinctive and diagnostic is not confirmed by other authors.

4. Diagnosis.

Darling and Fletcher mention the necessity to differentiate the condition from lichen planus, which shows inflammation, leuko-

plakia, which also shows inflammation in the corium, and thrush, which is distinguished by smears and culture, and rarely by histologic examination.

Zegarelli et al state that this lesion must be differentiated, particularly from "the tobacco pouch" lesion of tobacco chewers, mainly by the histologic features of the latter, which may show dyskeratosis.

As mentioned earlier, Smith considers careful supervision is necessary.

McCarthy and Shklar state that diagnosis is made on the basis of the clinical appearance of the lesion and the case history. Examination of the parents and siblings should be carried out if possible. Biopsy procedures are not indicated, since the microscopic picture is essentially nonspecific. Leukoplakia can be ruled out on the basis of clinical appearance and age. In these young patients, local oral irritation is minimal and smoking is obviously rare.

Keratosis Follicularis.

(Darier's Disease; Darier-White's Disease).

This is a dermatologic disease that appears to be inherited, at least in some instances, as an irregular dominant trait. (This condition is described only by Gorlin and Chaudhry, 1959, Shafer Hine and Levy, 1963, and McCarthy and Shklar, 1964. The descriptions by the first two authors are almost identical).

Clinical Features.

The cutaneous lesions are small, firm papules, red at first, then characteristically become greyish-brown or even purple, crust, ulcerate, coalesce and become verrucous and foul-smelling. They are generally distributed about the forehead, neck and over the shoulders, but, according to Allan (quoted by Shafer, Hine and Levy), they spread to the limbs, chest and genitalia.

According to McCarthy and Shklar, the disease generally is slowly progressive, although there is no relationship to the patient's general health. Exacerbations associated with a foul odour and secondary infection are common during warm, humid weather. Remissions with almost complete clearing are frequent during the winter.

Oral Manifestations.

The oral mucosa is probably more commonly involved than generally realized, according to Gorlin and Chaudhry, who found a number of reports of oral lesions in the literature. In addition, they pointed out that other mucosal surfaces such as the vulva,

pharynx, and larynx have also been reported as sites of the disease. Mucosal lesions, however, are generally apparent only when there is extensive skin involvement. The oral lesions appear as minute, whitish papules which feel rough on palpation. They are most frequently found on the gingiva, tongue, and hard and soft palates.

McCarthy and Shklar state that mucosal involvement in Darier's disease is rare. In the few patients where oral lesions were observed, a papular eruption was present. This occurred on the palate and consisted of a diffuse nodular reaction with light-brown firm lesions. Other areas such as the tongue and buccal mucosa may be involved.

Histological Features.

The disease is misnamed, since changes are not restricted to the hair follicles. Characteristic findings are hyperkeratosis, papillomatosis, acanthosis, and a peculiar benign dyskeratosis. The latter is characterized by rather typical cells called corps ronds and grains. The corps ronds are larger than normal squamous cells, and have a round, homogeneous, basophilic nucleus with a dark eosinophilic cytoplasm and a distinct cell membrane. These are found usually in the granular layer and the superficial spinous layer. The grains are small, elongated parakeratotic cells situated in the keratin layer. Both corps ronds and grains represent partially keratinized cells and are found also in the typical slit-like intra-derma vesicles, or lacunae, found just above the basal layer of cells,

the typical suprabasilar cleavage. The microscopic features of the oral lesions are identical, except that the hyperkeratotic changes are generally not pronounced.

Treatment.

Treatment usually consists in the administration of vitamin A, but the results are variable.

Hereditary Benign Intraepithelial Dyskeratosis.

Witkop et al (1960) reported this unusual hereditary syndrome discovered in 1954 in a racial isolate group of mixed Caucasian, Indian and Negro ancestry living in North Carolina. The syndrome is characterized by intraepithelial dyskeratosis of the oral mucosa and the conjunctiva, these sites of involvement being invariably associated.

Oral Manifestations.

These are generally white, spongy, macerated lesions of the buccal mucosa, with or without folds. They vary from delicate, opalescent white membranous areas to a rough, shaggy mucosa. The lesions frequently involve the corners of the mouth and appear as soft plaques with pinpoint elevations when the mucosa is stretched. Other areas of the mouth affected are the labial mucosa, floor of the mouth, and the lateral border of the tongue. The oral lesions resemble familial white folded dysplasia.

Eye Involvement.

The lesions of the eye are characterized by superficial, foamy, gelatinous white plaques overlying the cornea, sometimes producing temporary blindness. The conjunctivae are usually intensely congested. The eye lesions in some cases show a seasonal variation, tending to appear or increase in severity in spring, and disappear sometimes by spontaneous shedding of the pseudo-membrane, in the late summer or fall.

Histologic Features.

Sections show thickening of the epithelium with pronounced hydropic degeneration. Also, numerous round, waxy-appearing eosinophilic cells resembling minute epithelial pearls are evident, the "dyskeratotic" cells. Witkop et al state that the condition can be diagnosed either by tissue section or Papanicolaou-stained smears of buccal mucosal or conjunctival scrapings.

Treatment.

No increase in the death rate or in death from neoplastic disease was found, so Witkop et al stated that the condition is benign. No treatment was indicated.

Pachyonychia Congenita.

This rare congenital anomaly was originally described by Jadassohn and Lewandowski in 1906 (quoted by Gorlin and Chaudhry, 1958, and McCarthy and Shklar). Gorlin and Chaudhry stated that no more than 12 cases had been cited in the domestic literature since. Of 11 cases, 7 were males. The condition is sometimes, but not always, familial.

Clinical Features.

There are dystrophic changes in the fingernails and toenails, hyperkeratosis or calluses of the palms and soles, follicular keratosis of the acneiform type particularly about the knees and elbows, and hyperhidrosis or excess sweating of the hands and feet. Dystrophic changes of the hair and cornea are also reported occasionally. Verrucose lesions may occur on the elbows, but are especially common on the lower extremities, about the knees, popliteal fossa, lower legs and ankles. Plantar bullae are not uncommon.

The nails may be abnormal at birth, or very soon after. It is not uncommon for skin lesions to appear when the child is 18 months to 2 years old, while some have been observed at birth.

Oral Manifestations.

According to Gorlin and Chaudhry, oral lesions are nearly always present. They are white, opaque thickenings which may be focal, involving only a portion of the buccal mucosa or tongue, or may be quite generalized, covering the entire mucosa of the tongue,

lip and cheek. Angular cheilosis is commonly present. White patches have been noted on the oral mucosa at birth in most instances.

Histologic Features.

The mucous membrane exhibits acanthosis and intracellular oedema or vacuolization of the spinous cells. Parakeratosis is evident. There are no features pathognomonic of the disease.

McCarthy and Shklar state that, from the few pathologic studies reported, no specific histologic findings are present, other than hyperkeratosis.

Treatment.

There is no treatment for the disease, which is not considered to be a serious condition, (Shafer, Hine and Levy).

Chemical Burns.

Clinical Features.

Chemical substances with caustic properties (acids and alkalies) will cause injury to the oral mucosa, for example, aspirin burn. The acetylsalicylic acid produces a coagulation necrosis of mucosa, which appears as a white patch. Other caustics, such as lye, will produce liquefaction necrosis of the mucosa and deep layers, (Orban and Wentz), 1960).

Thoma and Goldman (1960) quoted Hirschfield (1939) who reported the following reactions from the use of sodium perborate:-

1. Painful burns of the oral mucosa; 2. A white discolouration of the epithelium, particularly the marginal gingiva; 3. Inflammation of the oral mucosa; 4. A form of hairy tongue.

Course of the Condition.

After application there is an inflammatory reaction, causing hyperaemia and oedema. The cheek, gingiva and tongue may become swollen and painful. The white slough gradually rubs off to reveal a red ulcerated lesion.

In aspirin, and other superficial burns, healing will occur in 5-7 days. In severe, deep burns, extensive sloughing of the tissues occurs with deep ulceration. Healing is protracted for weeks and finally occurs with scarring.

Differential Diagnosis.

Orban and Wentz mention the need to differentiate chemical burns from; 1. Hyperkeratosis, 2. Lichen Planus, 3. Erythema Multiforme 4. Bullous lichen planus.

Burket (1961) states that the diagnosis is made on the history of development, duration, appearance, and physical characteristics of the affected tissues. The coagulum can usually be removed fairly readily. Differentiation must be made from moniliasis, leukoplakia, and lichen planus.

Aetiology.

Orban and Wentz list the following causes;

<u>Self-medications.</u>	<u>Accidental or Suicidal Use.</u>	<u>Accidental Dental Applications.</u>	<u>Occupational.</u>
1. Aspirin.	1. Lysol	1. Phenol	1. Acid Fumes.
2. Silver Nitrate.	2. Phenol	2. Trichlorac-	
3. Tincture of iodine.	3. Lye.	etic Acid.	
4. Full-strength irritating mouth- washes.	4. Mercuric Chloride.	3. Silver Nitrate.	

Thoma and Goldman (1960) add to these, sulphathiazole, and self-curing acrylic resins.

Burket mentions also chromic acid, beechwood creosote, pure eugenol, 70% alcohol, snuff, or chewing tobacco, (as an initial reaction; if continued for long, hyperkeratotic changes may develop).

Shafer, Hine and Levy (1963) illustrate pyrozone and chloral hydrate burns, and state that any strong acid, alkali, germicidal agent, strong counter irritant, or even certain plant or animal irritants may produce injury.

Colby, Kerr and Robinson (1961) mention also Zinc Chloride.

Histologic Features.

According to Orban and Wentz, there is destruction of epithelium, and peeling off of the surface layers. There is an accumulation of large numbers of leucocytes below the burned surface, and this forms a line of demarcation between necrotic and living tissue. Sloughing of the necrotic area will occur, and the resulting ulcer is covered by a fibrinous exudate.

Treatment.

Bernier (1959) stated that the primary cause must be eliminated at once. Secondary infection is the greatest problem, and must be controlled by careful local measures such as cleansing of the lesion to remove necrotic tissue, and the judicious application of mild antiseptics. Penicillin (intramuscular for preference) may be employed to control infection if it is serious. Local irritating factors (e.g. dentures) should be removed.

Orban and Wentz list the following measures:-

1. Mild, soothing mouth rinses, such as sodium bicarbonate;
One teaspoonful in a glass of warm water.
2. Anaesthetic mouth rinse;

R~~X~~

Benzocaine 5 gm.

Emulsion of sweet almonds 2 ml.

Tragacanth (powdered) 2 gm.

Water q.s. ad. 100 ml.

sig : Use a few drops as an anaesthetic mouth
rinse before meals.

3. Benzocaine lozenges for pain.
4. Karo syrup in water; rinse to coat sore areas.
5. Hydrocortisone ointment to combat the most acute symptoms (2.5% hydrocortisone acetate ointment).
Apply locally for a few days only.

Burket recommends a mild antimicrobial agent (Metaphen, Zephiran Chloride Tincture 1:1000) or a mild antimicrobial agent with a surface anaesthetic (Butyn 4%, Metaphen 1:1500).

McCarthy and Shklar (1964) state that therapy involves neutralization of the chemical substance if possible, relief of pain and promotion of normal healing. Pain may be severe and a narcotic such as codeine is indicated. The areas should be cleansed and covered with an adherent paste containing a corticosteroid such as triamcinolone.

Thermal Injuries.

Extensive thermal burns do not often occur in the oral cavity, principally because of its inaccessibility to most of the severe thermal hazards. Minor burns, as from very hot beverages or foods, occasionally occur on the palatal or labial mucosa, even though this tissue is somewhat protected from thermal injury by its moist surface. Burns of varying degree may result from careless application of the cautery, using dental instruments which are too hot, dropping hot wax on the tissues, or using impression material which is too hot. Colby et al (1961) include an illustration of white coagulation of the gingival mucosa resulting from taking an impression with hydrocolloid material which was at a temperature sufficiently high to injure the tissue. Within 24 hours all of the coagulated material sloughed, exposing the underlying bone.

Treatment.

Healing is usually uneventful. The ulcerated area should be covered with a thick paste. Triamcinolone may be used in an adhering paste or in an ointment, and then covered with the adherent paste. Complete healing of an ulcerated area caused by a thermal burn usually takes approximately two weeks. The pain of the lesion is relieved considerably by the application of the paste. Codeine may be necessary for relief of pain during the first day or two following the injury, (McCarthy and Shklar).

Cheek, Lip and Tongue Chewing.

Colby et al (1961) state that a soft, linear streak of parakeratin, seen in the buccal mucosa at the occlusal line, is frequently termed linea alba. These lesions usually occur in individuals with thick cheeks that are closely adapted to the buccal surfaces of the teeth. The line may be initiated from irritation from rough buccal cusps. This condition may be intensified by the habit of sucking and chewing on the cheeks.

Burket (1961) comments that cheek-biting is usually seen in nervous adolescents and young adults. The involved areas have a milky white, rough, macerated appearance. The lesion is diffusely outlined, and frequently is limited to one cheek. Similar habits may affect the lips and tongue. Burket classifies these lesions as being not associated with hyperkeratosis. He recommends enlisting the co-operation of the patient (who is usually unaware of the habit) in eliminating the habits. Positive suggestion therapy may be helpful. At times, another habit, which may be less objectionable (e.g., chewing gum) may be temporarily introduced.

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