

5. Therapy of Papillomas.

All writers reviewed recommended surgical excision. Tietze, and McCarthy and Shklar emphasised wide excision, the latter feeling that irradiation is helpful in cases of doubtful malignancy and they stated that "biopsy is mandatory". Shafer et al stressed that the pedicle must never be cut through in the hope that this action will suffice. Miller (1957) stated that true papillomas are usually pedunculated and felt that they do not recur after removal, which statement had been made by Mead in 1940.

B. MULTIPLE PAPILOMAS (Papillomatosis) AND INFLAMMATORY PAPILLARY HYPERPLASIA

1. General

Bernier (1955) and Thoma and Goldman (1960) named the occurrence of multiple papillomas, usually on the hard palate, as "papillomatosis". They are usually discrete, small, firm, round tumours, are sessile and occur mostly under a denture relief area. They can so cover an area that they seem to be one lesion. Thoma and Goldman stated that a papillary condition may be caused by chronic irritation, in which case the author prefers the term "inflammatory papillary hyperplasia" or if the little projections are true neoplasms, the above term "papillomatosis" should be the one of choice.

Shafer, Hine and Levy used the two terms synonymously and while this writer does not agree with this, the literature uses the description of palatal involvement so loosely that it is impossible to say, quite often, what is the basic nature of the whole lesion, i.e.

neoplastic or hyperplastic (epithelial or connective tissue type) or both. In any case, this author, in doubtful cases, would advise biopsy, as malignancy has been connected with palatal conditions of this type.

Riga's disease refers to multiple papillomas on either side of the frenum caused by irritation of coughing in pertussis (whooping cough) in children. The tumours may be single or multiple and may become malignant, which is indicated by increasing growth, induration and fixation of the base and ulceration. The author feels that the usual initial lesions in this condition would be ulceration.

2. Observations on Papillary Conditions.

Thoma and Goldman pointed out that it is important not to confuse stomatitis nicotina with multiple papillary palatal lesions. In stomatitis nicotina, pseudopapillary formation is seen on the palate of patients wearing no dentures or in places not protected by a denture, due to formation of small cysts in secretory ducts of the palatal mucous glands and generally associated with hyperkeratosis, (See chapter on "Hyperkeratoses").

Salman and Langel (1954) asserted that hyperplasia is the most prevalent type of tissue growth seen in the mouth and forms at the site of chronic irritation. They said that chronic irritation in the palate can lead to malignancy.

Shafer et al (1963) have noted papillary lesions in the palates of people with their own teeth and wearing no prosthesis. The author feels these could be either of the two types (i.e. neoplastic or hyperplastic): neither is specified by the authors. Shafer et al

described the lesions as closely arranged papillary projections often involving nearly all of the hard palate and imparting a "wartlike" appearance, individual projections being seldom over 1 to 2 mms. in diameter. There can be varying degrees of inflammation, but ulceration is rare. They also warned of possible malignancy. Waite (1961), too, described papillary hyperplasia of the palate due to denture irritation and warned of its possible malignancy. Thoma (1952) had described a case that in the opinion of Goldman, Wolbach and Warren was histologically benign, but in Bernier's opinion was pre-malignant. Clinically, Thoma himself had considered the case malignant. It was a hyperkeratotic papillomatous palatal outgrowth almost covering the entire palate and Thoma named it "malignant papillomatosis of the palate". Colman, too, in 1951 had reported a case of a 66 years old white woman who had multiple excrescences on the buccal mucosa, which had been present for many years. They were gleaming smooth white masses from 1 to 10 mm. each in diameter and covered a great part of the buccal mucosa. They were flat and ovoid in shape. Many appeared confluent, but examination revealed that they overlapped slightly and that each was separate, being attached to the underlying mucosa by a broad pedicle. As the histopathology was indicative of nothing specific, a possible diagnosis of multiple polyposis with keratotic change is suggested by the author; but there was some epithelial abnormality and consequently, regular examination of the condition should be undertaken.

Donohue (1957) also reported a case of palatal "papillomatosis"

(as he called it) in a 78 years old woman who was poorly nourished and debilitated. The condition was present also on the upper lip and alveolar ridge and was continuous with the palatal involvement: this "extension" from the palatal section was caused, said Donohue, by the undernourished state, but was started originally by poorly fitting dentures. He diagnosed the condition clinically as a white fungating carcinoma, with a fur-like appearance. The lesion had been present for about 6 months. Donohue felt the condition was histologically consistent with pseudo-epitheliomatous hyperplasia. It was diagnosed histopathologically by Toto as verrucal inflammatory hyperplasia with malignant degeneration; by Tietze as hyperplastic oral mucosa with "leukoplakic" change; and by Bernier as "leucoplakia".

The confusion in terminology previously mentioned, and the brief descriptions just presented, explain why the author feels that cases of inflammatory papillary hyperplasia and papillomatosis should not be taken lightly.

Robinson (1957) stated that the weight of evidence points to the fact that papillary hyperplasia can become malignant. However, Halperin (1957) declared that the true papilloma of the palate (and this would, of course, apply to multiple papillomas), as distinct from the papillary hyperplastic lesions, is white (where the latter are red), may be flattened and should be totally excised, a biopsy being performed to make sure of the diagnosis and to confirm complete removal.

Most cases of inflammatory papillary hyperplasia of the palate are either completely or partially eliminated by the discontinuance of the wearing of the denture, the presence of which is usually associated

with the inflammation and this is emphasised by Fisher and Rashid (1952) who felt that in diffuse papillary hyperplasia "the fundamental process of inflammation" is caused by chronic excessive retention of food debris and stagnation of oral secretions.

The author does feel, though, that very few of these cases would present as white lesions. The point is that they can do so, as reported in this section, the diffuse, red, inflammatory hyperplastic condition becoming hyperkeratotic or the true multiple papillomas presenting their white clinical appearance "due to the thickness of the epithelium, lack of blood vessels and wide parakeratotic layer" (Orban and Wentz).

3. Histopathology

Inflammatory Papillary Hyperplasia. Thoma and Goldman described this condition as presenting numerous papillary projections of hyperplastic squamous cell epithelium, either keratinised or not. Fisher and Rashid (1952) found hydropic degeneration in all sections of the condition which they examined. The corium was loose, fibrous connective tissue, with variable oedema. An inflammatory infiltrate of lymphocytes and plasma cells is a feature, sometimes accompanied by leucocytes.

Papillomatosis, said Thoma and Goldman, can show pseudoepitheliomatous hyperplasia of epithelium. It has, therefore, a non-malignant appearance; however, mitotic figures (especially bizarre), areas of cells with hyperchromatic nuclei or vacuolization, loss of polarity between cells and generally, areas of dyskeratosis, may indicate pre-malignancy and careful watch must be kept on such a condition.

Waite (1961) stated that these conditions warrant biopsy.

4. Therapy

Waite (1961) recommended surgical excision in malignant or pre-malignant cases, after which the leaving out of any denture for a period of time would be advantageous. The condition can be removed down to the bone, including the periosteum if necessary, but this would, of course, delay healing. Such treatment was also advocated by Thoma and Goldman, who stated that electrocoagulation or irradiation could be used in addition.

C. SOME BENIGN TUMOURS OFTEN TERMED "PAPILLOMA"

1. The Polyp:

Salman and Langel (1954) described the fibrous polyp as resembling the papilloma or fibroma, except for a soft texture. They stated that the usual polyp was a finger-like projection of fibrous tissue with overlying mucous membrane of normal colour: it is usually pedunculated, but could be sessile, being found in the same sites as the papilloma and would not recur if thoroughly removed.

2. The Fibropapilloma:

is described by Thoma and Goldman (1960) as being usually larger than the papilloma, as it contains large amounts of fibrous tissue. They stated that there is no neoplasia of fibrous tissue in this outgrowth, the latter process being hyperplastic or inflammatory. However, the epithelium has undergone neoplastic change.

3. The Fibro-Epithelial Lesion:

or irritation (traumatic) fibroma is the most common lesion arising from the buccal or labial mucosae, being tiny or as large as

2 cms. in diameter (Gorlin, 1957). There appears to be a definite relationship of this tumour to trauma, but Gorlin felt that this has not been definitely established. It may be keratinised, but cannot be shown to be different histologically from normal mucosa or true fibroma. Gorlin also felt that;

4. True Fibroma is far less common than cited in routine surveys. Other tissues may be alloyed, producing the lipo-fibroma or osteo-fibroma, a myxomatous change also being sometimes seen.

5. The Epulis:

Salman and Langel (1954) stated that hyperplasia is the most prevalent type of tissue growth seen in the mouth and forms at the site of chronic irritation; it is seen frequently in the upper anterior region of the mouth in the labial sulcus. Bradley (1944) had said that hyperplasia frequently occurs in the oral cavity and that localised hyperplasia, such as that described by Salman and Langel, could be caused by a denture.

Thoma and Goldman (1960) described several types:-

- (1) Epulis granulomatosa
- (2) Gingival hyperplasia
- (3) Alveolar hyperplasia (epulis fissuratum)
- (4) Palatal hyperplasia.

The "epulis" is described by Salman and Langel (1954) as painless and seldom ulcerated. It may be single or multiple; it has a sessile base and the mucosa is normal in colour. Nathanson (1951) pointed out that this condition, when acute (recurrent), was not white, but red in colour: The author has seen cases of "epulides" in association with

hyperkeratotic areas. Epulides can grow to a large size, but Salman and Langel state that they have never seen a case become malignant.

Bernick (1948), in reviewing the literature on the subject, concluded that there should be uniformity in the use of the term "epulis". He felt it should describe a condition of hyperplasia, one which could be said to be between inflammation on one hand and neoplasia on the other. He presented figures for the sites of occurrence of the hyperplastic lesions, rating the maxilla as being more involved than the mandible. The writer feels that the wearing of dentures contributes to most cases of soft tissue hyperplasia of this kind in the mouth and as a denture is more likely to be worn in the maxilla, there could be expected a higher involvement here.

Histopathology of the Epulis: Bradley, and other authors reviewed, described a picture of vascular connective tissue, infiltrated with lymphocytes and plasma cells, with polymorphs present, but the presence of eosinophils a rarity. The epithelium is a well differentiated squamous type, but there is usually an inflammatory proliferation of this epithelium, long rete pegs extending into the underlying tissue. Round cell infiltration can extend into the intercellular spaces of the epithelium and there is often evidence of surface ulceration. In Epulis fissuratum, there is usually a dense infiltration of leucocytes in the valley between two folds of hyperplastic mucosa. Keratinisation can occur.

Therapy: The therapy advocated is the removal by surgery of the

excess tissue (folds), after which the denture, with a "compound" overlay where the flange has been previously cut back, is reinserted, thus acting as a splint. The patient should be seen daily until healing is well under way.

D. THE WART: (Verruca Vulgaris, Verruca Acuminata)

1. Description.

McCarthy and Shklar (1964) stated that "warts or verrucae are a specific viral infection of the skin and mucous membrane, characterised by a local epithelial hyperplasia". They may assume different clinical types often depending on the location. Moist warts are known as verruca acuminata and these may occur orally. McCarthy and Shklar observed that warts of the oral mucosa are very common to-day, whereas a little while ago they were unusual - they do not explain why, but this writer wonders if this could be concerned with an upset in symbiosis of the oral flora which results in:-

1. Increase in the causative viral agent
and/or

2. Change in tissue resistance.

Oral warts occur mostly in children, possibly because of a wart-laden finger being placed in the mouth.

Thoma and Goldman (1960), however, wrote that hard papillomas must not be mistaken for warts of skin, known as verruca vulgaris, which are of infectious nature. One infers that they did not believe in the existence of oral warts. Willis (1960) stated that infective papillary overgrowths of the epidermis such as warts or venereal

condylomas are not true tumours, but does not mention their occurrence in the mouth. Burket (1961) felt that warts of viral aetiology are also found in the mouth as well as on the skin, and can simulate the luetic condylomas.

2. Aetiology

Lyell and Miles (1951) wrote of Type I warts which are set deeply in the skin "like an iceberg floating in water", but Type B floating "like a cork on water". The author emphasises that they were dealing with skin, not oral mucosa.

Inclusion bodies were found in Type I (inclusion) warts but not in Type B (banal) warts. The inclusions were eosinophilic and were found in the nucleus and protoplasm of the epidermal cells, appearing first in the lowest prickle cells and affecting finally the cells of the stratum corneum.

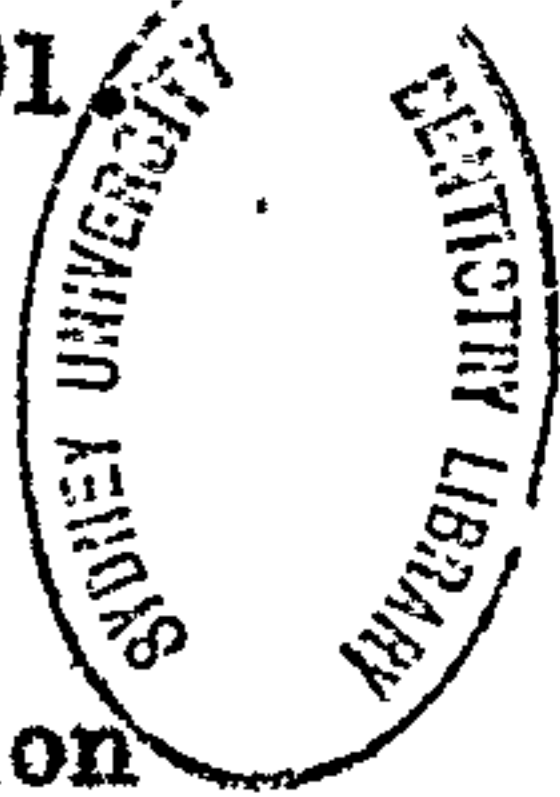
Bunting et al (1952) stated that certain warts differed clinically from other warts from the same sites, in that they had a smooth margin, relatively less keratinisation and a surrounding erythematous inflammatory halo. Warts of this type alone yielded in their suspensions, spherical virus-like particles under the electron-microscope and also possessed intra-nuclear inclusion bodies and characteristic cytoplasmic masses which the others lacked. The effect of viruses generally, they said, is apparently characterised by either necrosis or stimulation, and warts, having long been known to be transmissible directly or by their filtrate, have been regarded as being caused by a virus, which acts as a stimulator. In "virus" warts, there is also a distortion in the orderly development and differentiation of the epidermal cells,

which is not present in warts of the type from which virus-like particles have not been obtained.

Bivins (1953) obtained an agent from a human wart which caused massive proliferation and "pearl" formation when inoculated on chick embryos. No virus-neutralising antibodies were demonstrated in the serum of the patient from whom the wart agent was obtained. The agent was filterable through a Berkefeld "V" candle, but not at all through a Boerner filter pad and it was a little susceptible to the action of terramycin, aureomycin and phenyl mercuric nitrate, but not to streptomycin. However, his experiments were not repeated and he did not comply with Koch's postulates. Since then, McCarthy and Shklar disclose that Mendelson and Kligman have been able to culture the virus wart on tissue culture composed of monkey kidney. Vaccine preparation, therefore, may soon be available for prevention.

3. Clinical Manifestations.

The Verruca or wart is a small, circumscribed auto-inoculable epidermal and papillary growth of variable size, shape and consistency. It may occur at the junction of skin and mucous membrane of the lip, but here it is not usually white (Thoma and Goldman). Bhaskar (1961) said the wart occurs on the lips and on the palate and is a sessile, soft, cauliflower-like lesion which is only a few mms. in size. McCarthy and Shklar (1964) reported wart occurrence on all areas of the oral mucosa, but the lips and the vestibule are the most common sites. They termed it "relatively soft", non-horny and white because of moisture intake, any trauma leading to "brisk haemorrhage". Warts



may be single or multiple and can coalesce. A typical manifestation is a larger wart surrounded by smaller satellite ones. Rapid growth is the rule and they can appear very suddenly, although the incubation period varies between 6 weeks and one year (Bhaskar). McCarthy and Shklar have seen warts usually as sessile lesions, but said they can be filiform or pedunculated. Most writers stated that the lesions may disappear spontaneously.

4. Histopathology.

McCarthy and Shklar (1964) described a wart as consisting of localised hyperplasia of epithelial cells with sharply defined borders, Bhaskar (1961) adding that the wart is a papillary lesion in which the epithelium is thrown into folds. Writers agree that there is parakeratosis of the stratum corneum alternating sometimes with hyperkeratosis, which keratoses can vary in thickness. The rete pegs are long and thickened, with those at the margins between verruca and normal tissues being "bent" in towards the lesion's centre.

Mitotic figures are usually present and often there is intracellular oedema of the cells of the stratum spinosum. The papillae are elongated and tortuous with dilated capillaries and lymphatics, together with varying numbers of chronic inflammatory cells. The basal layer is intact (McCarthy and Shklar).

Certain cytologic characteristics distinguish those warts from which virus-like particles have been obtained. These are eosinophilic intra-nuclear inclusion bodies and vacuolated cytoplasmic masses in the cells of the epithelium that are absent in the warts from which the particles have not been obtained, in spite of similarity of the

papillary structure in both (Bunting et al, 1952). They also noted that nuclear enlargement and distortion, an absence of mitotic figures and interference in the development of the epidermal cells probably reflect the effect of the virus. McCarthy and Shklar stated that Bunting had found such inclusion bodies, but neglected to state that these inclusions had been found to be eosinophilic, McCarthy and Shklar themselves having stated that the inclusion bodies in the nucleus of the epithelial cell, when stained with haematoxylin and eosin, were basophilic. "Cytoplasmic granules" have been labelled "inclusion bodies" quite erroneously by some.

5. Diagnosis and Differentiation (Warts)

The rapid appearance of warts, the lack of depth and induration, is very characteristic, and a diagnosis of "wart" is especially emphasised by the presence of other warts on the lips and fingers (McCarthy and Shklar).

These writers believe that the usual appearance clinically of a papilloma is "smooth-surfaced", but the author feels this would be a very poor method of differentiation from the "rough-surfaced" wart, the same argument also applying to the fibroma and possibly a granulomatous lesion. Epidermoid carcinoma can only be eliminated by histological examination, which nearly all writers emphasised should be performed for both warts and papillomas, - (presuming that the two latter conditions are distinct).

6. Therapy.

Thoma and Goldman stated that removal is best accomplished by

the electrothermic method, while Burket favoured excision and cautery. McCarthy and Shklar also favour excision, but recommended podophyllin, a mitotic suppressing drug, as being very successful in a 20 per cent alcohol vehicle, applied direct to the wart. One treatment only is usually all that is necessary, but the application may be repeated in 7 to 10 days, until the wart disappears. Light desiccation and curettage under local anaesthesia is a popular and usually successful therapy. They discouraged ionizing radiation in treatment. Bhaskar said excision is good therapy, but mentioned the possibility of auto-inoculation.

E. MOLLUSCUM CONTAGIOSUM

This is a summary of the condition, found in McCarthy and Shklar (1964), who state that this lesion is very rare on the oral mucosa. It is caused by a virus which is the largest of all true viruses affecting man, being about 300 μ . It can be seen with a light microscope.

The lesions are globular and sessile, but flatten out later and become umbilicated. They have been seen on the tongue and the lips.

Histologically, the lesions are "striking", with molluscum bodies seen, representing degenerating epithelial cells. The basal layer is intact, with two or three layers of cells above it. In each cell, the "molluscum body" is formed by the forcing to one side of the nucleus by a homogeneous eosinophilic inclusion body. The stratum granulosum is thickened and there can be considerable hyperkeratosis. The inclusion

bodies are eosinophilic in the Malpighian area and basophilic in the horny layer.

Therapy: Merely piercing the tumour with a sharp instrument is usually enough to cause a deterioration and eventual disappearance, or the lesions may be excised.

F. MOLLUSCUM PSEUDOCARCINOMATOSUM

(Molluscum Sebaceum, Keratoacanthoma, Self-healing Epithelioma, Verrugoma, Pseudoepitheliomatous Hyperplasia)

1. Definition and Aetiology

This condition was well recognised in Britain in 1936 as an entity, Beare (1953) stating that MacCormack and Scarff had described it first.

Burman et al (1958) said that the name "molluscum sebaceum" was suggested in the belief that the lesion arose from inflammation and hypertrophy in sebaceous glands. The term has been used interchangeably with molluscum contagiosum (q.v.) an entirely different "skin" lesion caused by a virus and containing demonstrable inclusion bodies. It is now generally accepted that the condition is of epidermal origin, they said, and probably is not derived from a sebaceous cyst. Musso (1951) held the opinion that the condition derived from sweat or sebaceous ducts and hair follicles, as none of the lesions had been seen lying deeper in the tissues than the normal limits of duct and follicle epithelium.

An aetiology viral in nature had been suggested, but Beare (1953) could not support this, as the lesions were usually single, more common in the aged and no transference from one to another or reproduction of

the lesion had (or has) been seen.

The lesion has been reported under such names as self-healing epithelioma, molluscum sebaceum, verrugoma, pseudo-epitheliomatous hyperplasia and molluscum pseudocarcinomatousum (Helsham and Buchanan, 1960), but a case they themselves reported was designated "kerato-acanthoma".

Burman et al (1958) felt that the term "kerato-acanthoma" is based on the microscopic appearance and describes, in their opinion, the common wart. Further, they said that "acanthoma" is employed not uncommonly by some workers to designate a well-differentiated epidermoid carcinoma. They preferred the term "molluscum pseudocarcinomatousum", although they feel it is unwieldy. However, it emphasises two important features, - gross appearance and clinical behaviour. The author agrees with them.

Musso's (1951) report of a case was followed by discussion which led the author to infer that it was considered that molluscum sebaceum and keratoacanthoma were separate entities, although very similar.

Grinspan and Abulafia (1955) stressed that, in their reports, they are not referring to secondary pseudoepitheliomatous hyperplasia when discussing this condition, which secondary type is of known causation, such as in blastomycosis, tuberculosis, syphilis, reactions to insect bites and ingestion of drugs (i.e. bromides and iodides), and the hyperplasia observed at the edges of a chronic non-specific ulceration. The author calls to mind the pseudoepitheliomatous hyperplasia of the tongue seen in cases of myoblastoma. They implied that experience would

be the most important factor in the differential diagnosis of molluscum pseudocarcinomatousum and cancer. Grinspan and Abulafia grouped the lesions of this type under the heading of idiopathic pseudoepitheliomatous hyperplasia, as distinct from the above secondary type.

2. Occurrence and Incidence

Burman et al (1958) stated that the condition occurs with equal incidence in males and females. It has always been reported in the white races, among the older age groups between the 5th and 7th decades. There are very few recurrences after excision (which they recommended).

Grinspan and Abulafia (1955) stated that solitary lesions usually appear after 40 years of age and predominate at about 60 years.

Beare (1953) called it a "common tumour" (not rare). In 3 years, 76 examples of skin involvement by "molluscum pseudocarcinomatousum" were studied at the Royal Victoria Hospital, Belfast; during the same period, eight times as many basal cell epitheliomata and twice as many squamous cell carcinomata of the skin were seen in the Dermatological Department. Of the 76, 35 were males and 41 were females.

Beare stated that MacCormack and Scarff had found that "both sexes were affected" and that Rook and Whimster had reported that "men were twice as frequently affected as women". Beare mentioned that others had reported large occurrences also.

The average age of Beare's cases was 55 years, and this is generally held as the most usual age of occurrence. However, many occurrences appeared in the 66-70 years of age group.

The most common skin site was on the nose and cheek area, but Musso (1951) felt the lesion could appear "on any part of the body".

Bhaskar (1961) said the lesion of the mucous surface occurs on the lip, the tongue and the alveolar ridge. Helsham and Buchanan (1960) stated that the lesion is relatively common, although its differential diagnosis is only recent; most of these lesions previously had been treated as malignant conditions. However, either it is very rare in the oral cavity or the condition has been mistaken, as suggested above, for squamous carcinoma, for there is very little written or reported concerning purely oral lesions.

3. Clinical

Bhaskar (1961) said the lesions may appear clinically as an ulcer, nodule or a plaque. Burman et al stated that the condition starts as a tiny painless papule which grows rapidly to achieve its maximum size in 6 to 8 weeks. Of Beare's 76 skin cases, 63 gave a history of 8 weeks' duration or less, but the rate of growth varied. However, the maximum size was between 1 and 1.5 centimetres in diameter. A case of Molluscum Sebaceum of the skin was described by Musso (1951), which grew to its maximum size in about 7 weeks and then regressed over the following 3 weeks, with no recurrence of the lesion 7 months later. Bhaskar also mentioned that the lesions seem to regress spontaneously. Burman et al said that after 4 to 6 months, the lesions usually have completely disappeared, except for a residual scar. They described the skin lesion as hard and fixed, whereas Grinspan and Abulafia described the skin lesion as freely movable on the deeper

tissues. The case in the mouth reported by Helsham and Buchanan was also fixed to the underlying tissue and most lesions resemble a verrucous condition, perhaps carcinomatous. Helsham and Buchanan described an oral lesion as "white and verrucous". Most give a history of prior trauma, of soreness to pressure and rapidity of growth.

Grinspan and Abulafia described three distinct clinical entities, also with some difference in the histological picture, adding that they can be identical, clinically, with squamous carcinoma:-

1. Verrugoma, a wart-like lesion with a papillomatous central zone, with an adherent scale.
2. Molluscum Sebaceum, an elevated nodule with a keratin filled crater.
3. Nodulo-vegetating type, which is a raised, mushroom-like growth, with surface lobulations separated by furrows resembling a vegetating papilloma.

Burman et al noted the second type, with its central crater filled with keratin, saying that on the skin it was covered with adherent, black-brown crusts quite different, they said, from epidermoid carcinoma, although the writer would doubt a differential diagnosis on these grounds alone.

Bhaskar stated that the lesions were locally infiltrating.

There are reports of lymphadenitis in the proximity of these lesions which has been proved to be due to associated inflammation and has not been shown to be due to invasion. Ackerman and McGavran (1958) reported 2 cases of pseudo-epitheliomatous hyperplasia complicated by marked infection which obscured the pathological and clinical findings. Both were treated as carcinoma but the lymph nodes showed no signs later of carcinomatous change. However, it is felt that this lack of

metastasis at the time is not necessarily an indication of benignity.

The principal differences between kerato-acanthoma (as Ackerman and McGavran refer to it) and carcinoma are (relating to the former):

1. The short period of growth;
2. The gross appearance;
3. The microscopic pattern, which lacks the ultimate criteria of malignancy.

Grinspan and Abulafia even stated that there is sometimes a familial history of occurrence.

4. Histopathology

The biopsy specimen may be impossible to interpret if only a small margin and considerable keratin are included in the specimen, (Ackerman and McGavran). Bhaskar said that, microscopically, kerato-acanthoma consists of marked epithelial proliferation and apparent "invasion" of underlying tissues. The epithelial proliferation superficially resembles a squamous cell carcinoma, but all the epithelial cells are normal and do not show dyskeratosis, which is the only criterion for differential diagnosis between this lesion and epidermoid carcinoma.

Grinspan and Abulafia said that histologic examination of the skin lesion reveals infiltrative squamous cell proliferation usually originating from hair follicles. There are no atypical changes in the cells.

Burman et al, Grinspan and Abulafia, Musso, and Whittle and Lyell mentioned that the basement membrane may not be intact, but may be interrupted by an inflammatory exudate (composed of histiocytes,

lymphocytes, plasma cells and often many eosinophils, with an occasional giant cell - Burman et al). Engorged vessels account for a pink-tinged halo sometimes seen around the tumour, on the skin at any rate. Large quantities of well-formed keratin are produced.

The writer does not feel confident that the lesion would be non-invasive if the basement membrane is not intact.

The three (3) types described clinically also differ slightly histologically:-

1. The verrugoma shows only little inflammation.
2. Molluscum sebaceum has associated with it small follicular keratinous cysts, with cornified centres, and
3. Nodulo-vegetating types have an over-all picture of heavier hyperkeratotic follicles infiltrating the corium, with dense inflammatory cell invasion and some micro-abscesses seen at the depths of the horny pearls.

All three, of course, show pseudo-epitheliomatous hyperplasia.

Whittle and Lyell (1952) reported two (2) cases of the condition, the clinical features of which were as previously described herein. They stated that "the histological features invariably suggest to the pathologist, unless he has been forewarned, a diagnosis of well-differentiated keratinising squamous carcinoma". In a discussion of the reports of Whittle and Lyell, attention was drawn by several workers to the very numerous and sometimes irregular mitoses, which they construed as a danger sign of malignancy; but if the epithelium is proliferating, this mitosis must be taking place and the author also feels that the rapidly growing epithelium may cause "breaks" in the

basement membrane.

It is well said that meticulous scrutiny of the multiple lesions from many areas failed to reveal criteria sufficiently convincing to distinguish, unequivocally, molluscum pseudocarcinomatousum from a low-grade, well-differentiated epidermoid carcinoma. It seems to be a lesion biologically benign, but histologically malignant (Burman et al).

5. Therapy

All literature on the subject of skin lesions of molluscum pseudocarcinomatousum stressed the better cosmetic result of treating the condition rather than allowing self-healing.

Skin lesions respond well to cutting off the top flush with the skin and affecting haemostasis with light cautery, which gives an excellent cosmetic result (Beare, Whittle and Lyell).

Helsham and Buchanan curetted their lesion and followed this by cauterisation of the base, without recurrence. Good results have been obtained by complete excision, or by freezing and curettage (Whittle and Lyell). The cure of skin lesions following irradiation, even biopsy, the administration of antibiotics and antisyphilitic drugs seems to the author to be nothing more than sheer coincidence, when the spontaneous resolution of these lesions is considered. All cases reported have responded to simple treatment with no recurrence, which Grinspan and Abulafia felt emphasises their benign origin.

G. VERRUCOUS CARCINOMA

1. Definition and Description.

This type of squamous cell carcinoma was first described by Ackerman (1948), who noted its occurrence mostly on the buccal mucosa and lower gingivae. Shafer, Hine and Levy (1963) said the cancer may also involve the palate and the floor of the mouth. The condition is exophytic and presents clinically as a papillary, or verrucous, mass of very slow growth. Ackerman said that slow growth, good differentiation, the verrucous character, the great extension if allowed to expand, and local invasiveness are characteristic, with local metastases rare and distant metastases nil.

Local recurrence was common if radiation and surgery, which Ackerman recommended, were inadequate. It could be associated with considerable infection; hence lymph glands were often swollen locally.

Ackerman and McGavran (1958) stated that verrucous carcinomata have a "classic evolution and an excellent prognosis". However, Colby et al (1961), while admitting that verrucous carcinomas have a better prognosis than other types, stated that the advantage may be somewhat offset by the fact that their true nature is not always suspected, clinically, until they have reached a large size.

Lucas (1964) and other authors reviewed on the subject, stated that this tumour occurs usually in elderly male patients, as do all types of squamous carcinomata, adding the tonsillar area as a site of occurrence to the sites stated previously.

Orban and Wentz (1960) described a lesion developing under a full lower denture on the crest of the ridge; it was a white verrucous

carcinoma. Lucas also described the lymph gland swelling due to infection, not metastases; Ackerman felt the verrucous carcinoma was unique in that it invariably grows around lymph nodes rather than metastasising to them. Ackerman and McGavran admitted, however, to three (3) cases of metastasis, though not stating at what stage in the disease the metastasis took place, i.e., whether the disease was in an extremely advanced condition. If this latter state prevailed and the condition was thought to be the usual squamous carcinoma, two incorrect courses could be followed:

1. A course of hopelessness, believing the disease to be past treatment.
2. A course where surgery is adopted, with radical neck dissection, unless there is definite evidence of lymph node involvement.

2. Aetiology

The aetiology has been described in the chapter on squamous cell carcinoma, but Ackerman noted the significance of tobacco chewing in association with the presence of this disease.

3. Histopathology.

Ackerman's description of the histopathology was that of a process of transition between atrophic epithelium initially, leading finally to the picture of the ultimate condition. Keratin formation was the first change, with accompanying club-shaped down-growth of epithelium, which latter was well differentiated and the basement membrane intact. Lucas added that epithelial pearls and small cysts are often seen, but

mitoses and cellular atypism are rare: there is always a heavy inflammatory infiltrate in the stroma. Ackerman described the inflammation as co-existent with the lesion and present beyond it, the infiltrate being composed of plasma cells, mononuclears and rarely, focal abscesses; he felt the inflammation probably affected the invasiveness. Shafer et al described the spinous cells as extremely well differentiated, showing little mitotic activity, pleomorphism or hyperchromatism; "One prominent feature found in most lesions is the thick strands of keratin deep in the tumour mass, especially in the crevices between the papillary projections." Orban and Wentz complete the description of transition by describing the elongated, irregular epithelial ridges penetrating deep into the connective tissue, and where hyperkeratosis is not present, small ulcers of the cauliflower-like surface may appear. Ackerman also noted cystic degeneration of the central "fingers", as proliferation continued.

The author can imagine the original atrophic epithelium becoming firstly hyperkeratotic and verrucous, or as Bhaskar (1961) called it, "verrucous leukoplakia". Bernier, in diagnosing several cases of possible molluscum pseudocarcinomatousum, had given a histopathologic diagnosis of "verrucous leukoplakia", which would seem to be hyperkeratosis complex with a papillary appearance. The latter appears to the writer to be a "stage" in transition of the disease, just as hyperkeratosis complex of the non-verrucous type may be a stage in the production of non-verrucous cancer.

4. Diagnosis and Differentiation.

The possibility of kerato-acanthoma being the actual condition rather than cancer should be kept in mind (Helsham and Buchanan). The author feels, as Lucas does, that probably kerato-acanthoma (molluscum pseudocarcinomatousum) has been diagnosed in the past as a carcinoma or even as pseudoepithelial hyperplasia. It is felt that the distinction between frank carcinoma, molluscum pseudocarcinomatousum, pseudoepitheliomatous hyperplasia and verrucous carcinoma would require experience and great care, and would depend on the combined histopathology and clinical findings.

5. Therapy.

Lucas, Ackerman and McGavran, Orban and Wentz all recommended complete removal by surgery with a wide margin of healthy tissue. However, this may be very difficult to accomplish without causing great disfigurement, for the disease may invade locally to a great degree, bone being also involved.

Conclusion.

More detailed description of carcinoma, yet still limited, owing to the restriction of manifestation as a white lesion, may be seen in Section 2.

SECTION 5.

DISEASES OF THE SKIN AND MUCOUS MEMBRANE

WITH WHITE ORAL MANIFESTATIONS

- A. PSORIASIS
- B. LUPUS ERYTHEMATOSUS
- C. LICHEN PLANUS
- D. LICHEN SCLEROSUS ET ATROPHICUS.

DISEASES OF THE SKIN AND MUCOUS MEMBRANES WITH WHITE ORAL MANIFESTATIONSA. PSORIASIS1. Introduction

Usher (1933) placed psoriasis of the mucous membranes among the rarest of the dermatologic conditions. He felt that its manifestation as a mucosal lesion had always been debatable and, to the present time, some deny its existence in this situation.

Mead (1940) defined oral psoriasis as another name for what he called "leukoplakia" (meaning hyperkeratosis) and this has been quite a common occurrence in the past. However, many years before Mead, Oppenheim in 1903 and Thimm, a little earlier, as quoted by Usher, had reported the first cases of true oral psoriasis which they had "confirmed" histopathologically. Both Oppenheim and Thimm had stressed the importance of the presence of parakeratosis, acanthosis and papillomatosis histologically.

Thereafter, further cases were reported, usually the patient having oral lesions situated in a linear region extending from the oral commissure to the 3rd molar area on the buccal mucosa, but very little of this was histopathologically confirmed psoriasis. Usher examined the buccal mucosae of one hundred consecutive patients with psoriasis, of whom only two were diagnosed as having oral manifestations of the disease. The author feels that it is very important to realize that Usher examined, as he himself stated, "the buccal mucosae" for psoriasis; apparently he felt that this would be the preferred area of occurrence - a presumption, possibly. Could it be that, having

examined the buccal mucosae and finding lesions there, he then proceeded to examine the rest of the mouth? If so, surely lesions could have been missed, for it was shown later that oral lesions are not confined to the buccal mucosa.

Scheer (1936) had noted the occurrence of what he designated "lichen planus" of the mouth occurring concurrently with psoriasis of the body and had also noted, as did Usher in one case, the appearance of "leukoplakia" orally in combination with psoriasis of the skin. Levin (1954) quoted Bernier, who, with other authorities, had the opinion that oral psoriasis is nothing more than "leucoplakia" in one of its varying stages of pathology.

Brayshaw and Orban (1953) also mentioned the reported findings of psoriasis of the oral cavity and felt that some cases may have been confused with lichen planus or "leucoplakia", as not all cases had been substantiated by histology.

The writer, in 1964, must agree with the statement of Usher 30-odd years previously, that psoriasis of the oral cavity is rare, for in both medical and dental writings, there is very little reported on this manifestation of the disease.

2. Occurrence

Shafer, Hine and Levy mentioned the fact that psoriasis is uncommon in children and primary attacks are rare after the age of forty five years. It occurs usually in the second and third decades, affecting either sex; all kinds and conditions of man are also equally involved.

Moyle (1936) found it interesting that in the majority of cases reported, the site of oral eruption had been the so-called "cutaneous

region" of the cheek. He stated that this region, according to Jadassohn, was closely associated with the skin and is the most common site for mucous membrane lesions of the cutaneous dermatoses (e.g. lichen planus). However, oral lesions have been reported to occur on the palate, lips, gingivae and floor of the mouth as well as the abovementioned buccal mucosa.

On the skin, lesions are most often found on the exterior surfaces of the extremities, elbows and knees, the scalp, the back, chest, face and the abdomen, with involvement of hands and feet being uncommon, except under and around the fingernails. It is said to be more severe in Winter, less so in Summer, and warmth and sunshine improve the condition. Arthritis is found, according to Shafer et al, quoting Allen, in approximately 12 per cent of patients.

The disease is not serious, leading, however, to cosmetic disfiguring in many cases.

3. Aetiology

Thoma and Goldman (1960) and earlier Levin (1954) had stated that the cause of the disease is unknown, but many investigators believe it must be caused by infection. This is confirmed in other writings (e.g. Shafer, Hine and Levy). Thoma and Goldman and Levin also added that there is a belief that the disease is due to a disturbance of fat-soluble vitamin metabolism, but Burks and Montgomery as far back as 1943 could find no evidence to support this theory: the vitamin theory of aetiology has therefore been in evidence for many years.

As for an aetiology of infection, Burks and Montgomery could

find no evidence of bacteria or fungi in any case of psoriasis, nor could they find any support for a virus aetiology. Levin felt the aetiology may be an allergic manifestation of a fungus infection.

In speaking of a psychic cause, Levin also mentioned climatic conditions as influencing the disease. Shafer, Hine and Levy stated that mental stress is invariably present to increase the severity of the disease and induce exacerbations. They mentioned the possible role in aetiology of endocrine dysfunction but said there is little factual basis for this argument.

Thoma and Goldman said that 30 per cent of cases have a familial history, with which Stones (1962) agreed, Levin having mentioned the occurrence of familial tendencies in 1954. Shafer et al, however, stated that a history of inheritance is "exceptional".

4. Clinical Manifestations

Psoriasis of the skin, according to Shafer, Hine and Levy, is characterised "by the occurrence of small, sharply delineated, dry papules, each covered by a delicate silvery scale which has been described as resembling a thin layer of mica. If the 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 skin is dusky red in appearance."

They said that skin lesions are painless, a little pruritic at times, and may be few, or very numerous and extensive. Small lesions can join to form large, irregular plaques, which may be symmetrical.

Oral lesions are either greyish-yellow-white plaques, silvery white areas with an erythematous base, multiple papules with

ulcerations, or small elevated papules with a scaly surface.

The first case of oral psoriasis reported by Usher (1933) was of a man, 24 years of age, a labourer. His attack was his third and of 3 months' duration, which improved in the Winter and regressed in Summer, - the opposite to the usual course. He had skin lesions. His tongue was scrotal, beefy red and enlarged. It was covered with papules which were themselves covered with a superficial layer of whitish epithelium which could be scraped away. However, under the tip on each side was a sharply circumscribed large oval plaque, reddish in colour. Opposite the upper right molars was a greyish-white patch on the buccal mucosa; the rest of the mouth was clear.

Usher's second patient had recurrences during Winter and remissions during Summer. She had marked cutaneous lesions on the body, scalp and extremities. The buccal mucosa was again involved in large lesions, this time each described as a fairly coarse, interlacing network of grey-white striae enclosing unaffected mucous membrane. The epithelium could be scraped away only with difficulty. The tongue and the palate were unaffected. The patient was a young girl. The diagnosis was made in this case entirely from the clinical course of the eruption, as the oral lesions revealed nothing specific from a histopathological point of view, even though the cutaneous lesions did show a typical picture of psoriasis. The coincidental appearance, however, of the lesions on the mucosa and on the body, their reaction to treatment with a gold compound (see "therapy") with no concurrent local therapy and finally their subsidence, appeared to Usher to substantiate the diagnosis of psoriasis. He had ruled out

keratosis as the patient was a very young girl, a very light smoker and there was no history of syphilis. The writer asks could this have been lichen planus?

Goldman and Bloom (1951) reported two cases of oral psoriasis, the first in a 63 year old man in whom there was an asymptomatic, slight thickening of the mucosa of the lower lip, of 2 months' duration. Examination disclosed a moderately indurated, raised, greyish-white, irregularly shaped plaque on the lower lip, to the left of the midline. There was no apparent ulceration and the patient had had a psoriasis of the skin for many years. A second case they observed was of a 28 years old male and revealed a rough lesion of the floor of the mouth, which lesion was raised and irregular, whitish and "fuzzy", extending under the tongue posteriorly. However, this case had no history of skin lesions until, at the time of oral examination, a lesion of the scalp was found.

The lesions in both cases, they felt, were quite unlike "leucoplakia" (hyperkeratosis) or lichen planus.

Brayshaw and Orban (1953), in a very lucid, concise report, gave descriptions of three (3) cases of oral psoriasis. In the first, a coloured man of 35 years of age, lesions of about 1 cm. in diameter, slightly elevated, were found on the papillary and attached gingiva bilaterally, just distal to the upper cuspids. Both showed Auspitz's sign and were slightly "itchy". However, the surface was scaly and glistening, with slight diminution in pigmentation (see Histopathology) - they were greyish-white. The patient presented no skin lesions.

In the second, a 33 years old male presented a white-grey crescent-shaped lesion on the attached gingiva over the upper left bicuspid. There was no history of this case available. The skin here was also clear of lesions. There was haemorrhage on contact. A third case was also reported, with a lesion on the gingival margin, between the upper bicuspids. It was an opaque whitish area of about 2 mms. in diameter and showed small, scale-like spots; no further details are given except that it resembled the oral lesions reported in other cases of oral psoriasis.

A case of Levin (1954) involved the soft palate - the sufferer was again a man, of 31 years of age, in good general health. The lesion was a firm, raised mass 3 cms. long and 1 cm. wide, involving the mid soft palate to the uvula, but not extending onto it. He did not mention its colour, but stated that it was multi-ulcerated - the posterior dorsum of the tongue had a black "hairy" appearance. The lesion was indurated. The throat was inflamed and jugular lymph nodes were enlarged on the right-hand side. There was also a skin eruption on both upper arms and body consisting of sharply defined, dry patches of erythema covered with silvery scales, with palpable lymph nodes in the axilla and inguinal region.

All possible systemic tests were essentially negative. A clinical diagnosis, confirmed by histopathology, was psoriasis, the condition remaining unchanged for eight years, but later beginning to worsen slightly.

He concluded that "in the presence of psoriasis of the skin, any

oral lesion should be thoroughly studied for a possible psoriatic granuloma," and with this the writer agrees, with the proviso that, as oral psoriasis is not a proven manifestation, a presumptive diagnosis should not be hastily made.

5. Histopathology

Shafer, Hine and Levy defined the most characteristic features of psoriatic lesions as parakeratosis with lack of hornification (a friable condition resulting), absence of the stratum granulosum and elongation and clubbing of the rete pegs. The supra-papillary epithelium is thin, and therefore bleeding points can be produced by scraping, which exposes the underlying corium, as the overlying epithelium is gradually removed. Dilated capillaries (or venules, as Bhaskar called them) are prominent in the papillae and the author feels that this is another reason why easy haemorrhage can be produced by scraping. Intra-epithelial micro-abscesses are produced (Monro's abscesses) and inter- and intra-cellular oedema of the stratum spinosum is usually present, as well as in the papillary layer of the lamina propria (Orban and Wentz). These authors also mentioned the presence of lymphocytes and histiocytes in the submucosa, but noted the absence or rarity of plasma cells. Polymorphonuclear leucocytes are present in connective tissue and in the abscesses, having migrated through the epithelium. They stated that air spaces in the lamellae between the parakeratotic surface layers produce the clinical silvery scales.

In Usher's first reported case, the histopathology revealed parakeratosis, the stratum granulosum was thinned or absent, the stratum spinosum was of normal thickness, but the rete pegs were

elongated and not thickened. There was a lymphocytic infiltrate around dilated blood vessels of the corium. Micro-abscesses were present in the epidermis and they contained round cells and polymorphonuclear leucocytes. There was an absence of plasma cells and collagen fibres were oedematous, but otherwise normal. The picture was certainly suggestive of a psoriatic lesion.

Burks and Montgomery (1943) stated that the histologic picture of psoriasis is usually diagnostic if a well developed, fairly recent plaque is examined, although an indolent skin plaque, they said, may be difficult to distinguish from other dermatites. There was no increase in skin lipid content, they said, and they found no evidence that psoriasis might eventuate in any type of lymphoblastoma or epithelioma, which had been an opinion held by some workers.

It seemed to them that the characteristic combination of changes consisted of uniform to spotted or layered parakeratosis, diminution or absence of the stratum granulosum, regional acanthosis, often with bulging of the tips of the rete pegs, mild intra- and less inter-cellular oedema, a varying degree of normal mitoses in the basal and prickle cells, uniform and regional papillomatosis with clubbing of the papillary bodies and thinning of the suprapapillary plates, dilatation and tortuosity of loops of the capillary vessels, a mild perivascular infiltration of lymphocytes and monocytes in the upper cutis and migration of polymorphonuclear neutrophils through the epidermis, resulting in microabscesses. Their findings therefore coincided with the aforementioned description of the histopathology

of the disease and they said that no other disease presents this combination of histologic changes. The author feels that this would be the ideal picture and it would be very fortunate indeed to view a section showing all these classical signs.

Burks and Montgomery reported a lessening of melanin formation in psoriasis, but no permanent disturbance in the formation was noted.

Goldman and Bloom's case of the psoriatic lesion of the lip showed hyperkeratosis and parakeratosis in alternating layers, with no micro-abscesses. The sub-epithelial tissue showed slight oedema and a perivascular inflammation composed chiefly of leucocytes, lymphocytes and some histiocytes. Numerous dilated blood vessels were present which, in some areas, became sinusoidal in character and roughly paralleled the basal layer of epithelium. There was, however, a complete lack of rete pegs, an unusual finding, it is thought, for psoriasis.

The second case of Goldman and Bloom revealed a papillomatosis of the epithelium with acanthosis, some parakeratosis and hyperkeratosis. However, the stratum granulosum was thickened, an uncommon finding in this disease, being four (4) or five (5) cells deep, while the epithelium over the papillae, which were clubbed, was very thin. Some intra- and inter-cellular oedema was noted. The usual histopathologic picture pertained in the corium.

The author feels it is noteworthy that neither case exhibited micro-abscesses of Munro and the second case showed hyperkeratosis and thickening of the stratum granulosum; however the investigators felt that both histological pictures were comparable to those seen in

psoriasis.

Apart from the presence in one case of some plasma cells and, in another, considerable desquamation (not unusual, and explaining the friability), Brayshaw's and Orban's cases showed a histopathology absolutely classical in type, pictures which the writer feels could be pathognomonic, though Bhaskar felt that the histopathology of this disease is never such (i.e. pathognomonic) and that diagnosis can only be made by concurrent appearance of skin lesions. Shafer et al felt that oral lesions of psoriasis "must be viewed with caution even though the histologic sections of the lesions do present a psoriaform pattern".

6. Diagnosis and Differentiation.

Burket said that biopsy is essential in diagnosis of oral psoriasis, for, without it, any definite statement would be presumptuous, if not impossible. Bhaskar, as previously mentioned, required lesions of the skin to be present to make a definite diagnosis.

In a case reported by Moyle (1936), both cutaneous and oral lesions were present. The oral lesions were brownish initially, however, turning darker and becoming more verrucose. They were situated on the hard and soft palates and were "rough" when first examined. Though local treatment was given to the skin lesions, no local treatment was given to those of the mouth. After two weeks, white lesions were noted on the buccal mucosa and he concluded this recent eruption was a symbiotic lichen planus. He could not explain the pigmented patches in the mouth. In discussion of this case, "lichenoid

psoriasis" was mentioned, the two diseases being thought to run concurrently. This case is one of several mentioned in the literature in which body or skin psoriasis has been linked with oral lichen planus, and certainly in differential diagnosis, this latter condition would have to be considered, together with the keratoses and chronic discoid lupus erythematosus and moniliasis; indeed, any white lesion would have to be "eliminated".

Levin (1954) said that the hyperkeratoses are common in the oral cavity, while psoriasis is usually not so - psoriasis occurring as an extension from cutaneous lesions; too, the hyperkeratoses are usually seen in old men. However, Brayshaw and Orban have given instances of no occurrence of skin lesions in oral psoriasis, the oral lesions being typical of the disease in every way. In psoriasis, too, lymph nodes may be involved, while this is not usually so in hyperkeratosis, unless the "complex" type is present. In any case, the histopathology is very different, there being few, if any, epithelial cell nests or pearls in psoriasis and the inflammation in the corium is usually quite different in type. The psoriatic oral lesions, of course, are more prone to spread if they are consistent with the habit of skin lesions (the author feels this is mere speculation). Levin also stated that there is pain in swallowing where oral psoriasis exists, which is not the case usually in hyperkeratosis.

But the important difference in the author's opinion would be the typical histologic picture, all things being equal.

7. Therapy

Stones recommended local application of tar preparations as "of value" - ultra violet light and irradiation, also, he felt are helpful, but Levin stated that radiation treatment is not recommended unless the disease is in a very early stage.

Sodium Arsenite by mouth gave good results in Usher's first report, but the mouth lesions reappeared. In his second case, Usher used gold-sodium thiosulphate intravenously to very good effect and, by inference, employing the results of therapy using this drug in the treatment of lupus erythematosus, one could conclude that the oral lesions were of lupus erythematosus rather than psoriasis; in addition, the patient was a young girl (see "Lupus Erythematosus") (Monash, and Prinz and Greenbaum).

The lip lesion of Goldman and Bloom was totally excised and normal healing resulted, a state of affairs which applied also to a gingival lesion in a case of Brayshaw and Orban, where no recurrence took place within nine (9) months after excision. Orban and Wentz said that patients with oral lesions alone have had no recurrence after excision.

Levin stated that penicillin had no beneficial effect, but that the use of aureomycin did halt the progress of virus infections associated with this disease and seemed also to diminish the intensity of pain. He found vitamins of little value, although Orban and Wentz said that Vitamins A, B complex and D₂ had been beneficial and that alcohol was contraindicated.

Irrespective of what drug was used, Levin felt that psychic supportive treatment of nervous patients was of great value, and he also recommended the excision of stubborn areas of involvement in the mouth.

All authors agreed that, as in lupus erythematosus (q.v.), ACTH has only kept the disease relatively quiescent.

Levin concluded that, though there is no specific treatment, enlightened and experienced management of psoriasis will keep the disease under control and prevent many troublesome consequences.

"Psoriasis of the Oral cavity", he said, "is more resistant to treatment (than skin lesions) and the least that can be hoped for is palliative relief".

B. LUPUS ERYTHEMATOSUS

1. Introduction

This disease belongs to a group called "the diffuse collagen diseases".

In 1941, Klemperer et al drew attention to the fact that the condition common to the multiplicity of lesions in disseminated lupus erythematosus was degeneration of the collagenous connective tissue in many organs, the same factor being present in polyarteritis nodosa, rheumatic fever, rheumatoid arthritis, serum sickness, diffuse scleroderma and dermato-myositis. Rich called these conditions "the collagen-vascular diseases." (cited by Boyd, 1963).

The most characteristic lesion in the diffuse collagen diseases is so-called "fibrinoid degeneration and necrosis" of connective tissue.

There are two components in this lesion:

1. A swelling of the ground substance
2. Separation of the collagen bundles which later disintegrate into granular material that finally merges into the swollen ground substance.

The necrotic material stains bright red with eosin and reacts with the special fibrin stains - hence fibrinoid necrosis or degeneration.

Whether fibrinoid material represents degenerated collagen, altered ground substance or simply fibrin deposited in the area is debatable. Mucopolysaccharide alteration is responsible for the intensely positive reaction with P.A.S. stain. On the other hand, Gitlen et al (1957) have shown that fibrin does exist in the fibrinoid material, which presence shows that there is a local conversion of fibrinogen into fibrin and suggests a local increase in vascular permeability, together with an abnormal release of thromboplastic substances into the area as a result of local tissue deterioration or necrosis. It was observed also that the conventional staining methods employed were not reliable for revealing fibrin in tissue sections, since they frequently gave negative results for areas in which fibrin could be demonstrated with specific fluorescent antibodies (see "Histopathology").

There is a third component of the lesion, namely, an inflammatory reaction to the primary connective tissue "injury".

Duff (cited by Boyd) says that differences in the above components, plus differences of anatomical distribution of the lesions, give the different collagen diseases their individuality.

However, the diseases do not necessarily have a common aetiology. There is a tendency to regard the presence of fibrinoid necrosis as an indication of an antigen-antibody reaction, allergic in nature in the tissue involved.

Boyd said that there is every reason to believe that the lesions of rheumatic fever and polyarteritis nodosa are manifestations of an antigen-antibody reaction in the target organs and therefore allergic in nature, but there is not any clinical evidence to say the same for disseminated lupus erythematosus, even though its clinical and pathologic manifestations are similar to known hypersensitivity reactions. However, experimental evidence seems to support the view that it is an allergic reaction.

Muir (1960) stated that in acute lupus erythematosus, the evidence of a supersensitive reaction of the auto-immunisation type is suggestive, but not proven.

Recently the L.E. cell phenomenon has been found in supersensitive reactions to penicillin and in patients receiving the drug Hydrallazine for hypertension. In the latter case, the clinical picture of acute lupus erythematosus has been closely reproduced, the patients returning to normal on discontinuation of the drug. All that can be said is that presumptive evidence for a supersensitive reaction in this group of diseases is strong, but as yet complete proof is lacking.

2. History

Sugarman (1953), in a history of the disease, stated that Brett, in 1828, first described symptoms which correspond with present-day lupus erythematosus. Wiener (1947) wrote that the term "Lupus Erythematosus" was coined in 1851 by Cazenave in a clear differentiation from other forms of lupus. Cazenave described this form of lupus as one which destroys superficially and which does not develop tubercles (or, as he meant, ulcerating nodules). Later, Kaposi in 1872, published a report of lupus erythematosus, using the term "Erisipelas Perstans Faciei" and as Damashek (1961) said, he (Kaposi) was the first to recognise the disease as an entity. But it was Jadassohn in 1904, who summarised the dermatologic observations and also called attention to acute lupus erythematosus as a serious systemic disease. As early as 1905 Osler, as reported by Sugarman and Stillerman (1960) had said, in describing "lupus erythematosus" as "Exudative Erythema", that it was a recurring disease, one which may not be characterised by skin manifestations and that the visceral symptoms may be present, yet to the outward view the patient may have no indications of "erythema exudativum" whatsoever.

There had been a following for the idea that tuberculosis may play a part in the aetiology, but this was "disproved" by Keil in 1933; yet Wiener, in 1947, stated that the role of tuberculosis in the aetiology of lupus erythematosus chronicus "remains controversial" and that many factors could change the character of the "chronic" into the "acute" form. The supposed "tubercular" role doubtless was

responsible for the use of the term "lupus" (a wolf) to describe the disease and there is no doubt that many sufferers from the disease (L.E.) had tuberculosis as well, although this applied mainly in Europe, whereas in the United States, lupus erythematosus was not usually associated with a tubercular infection.

It was later shown that the heart, the blood vessels, serous membranes, lymph nodes, indeed most tissues, could be affected, until in 1941, Klemperer et al stressed the collagen changes as evidenced by fibrinoid degeneration. Different types of lupus erythematosus had been noted, and McCreight and Montgomery (1950) showed that it was impossible to distinguish these types solely by histopathological methods.

The lupus erythematosus (L.E.) phenomenon was first demonstrated by Hargraves (1949), as cited herein by Sugarman (1953), and it was Haserick (1951) who discovered that the blood of patients with lupus erythematosus contained this L.E. factor which can be detected by adding the whole plasma of the patient to preparations of human or dog bone marrow. The L.E. factor/phenomenon has had an enormous impact on diagnosis of lupus erythematosus and will be described in the section on "Diagnosis".

3. Classification.

McCarthy and Shklar (1964) stated that classification is perhaps the most critical point in the evaluation of the disease, comparing it, in this sense, with pemphigus, a statement which, after reading the literature, the writer heartily confirms.

The classification used by Silvers (1950) is a widely accepted one and it embraces four (4) types of lupus erythematosus:-

1. Acute disseminated lupus erythematosus
2. Subacute disseminated lupus erythematosus
3. Chronic disseminated lupus erythematosus
4. Chronic discoid lupus erythematosus.

Silvers suggested that there should be a distinction between the disseminative types that show systemic involvement and not necessarily characteristic cutaneous lesions and the localised variety which has no demonstrable systemic disturbances but has characteristic cutaneous manifestations. Some investigators go further and state that, despite the same basic nomenclature, the discoid form of the disease is not related to the disseminated form, i.e. Streaan (1957).

Barnett (1961) quoted Wiener, whose classification of lupus erythematosus is as follows:-

1. The cutaneous form
2. The systemic form
3. The cutaneous form with systemic exacerbation.

He felt that the cutaneous or chronic discoid form was related to the disseminated or systemic form and that this former type may exacerbate systemically, a complication which is not, he felt, as serious as the primarily systemic type.

Weiss and Swift (1955) stated that discoid lupus erythematosus can become disseminated and avowed that this is "accepted fact".

If this can happen, the writer feels that there would be some connection between the two basic types, cutaneous and systemic, and

this seems to be the opinion presently held by many workers, including Archard et al (1963).

However, McCarthy and Shklar feel that the chronic discoid type does not progress to the systemic form, feeling that a wrong initial diagnosis (of chronic discoid instead of disseminated) is the reason for this "mistaken" idea.

Rost (1959), as well as Cook (1958) and recently McCarthy and Shklar, differentiated three types:

1. An acute disseminated lupus erythematosus,
2. A sub-acute disseminated lupus erythematosus,
- and 3. A "fixed" or chronic discoid lupus erythematosus.

Apparently, they do not recognise a chronic disseminated form.

Rost felt that the term "lupus erythematosus" should be abandoned and replaced by "erythematoes discoides" for the chronic discoid form and "erythematoes disseminatus" for the acute disseminated form. The traditional adjective "erythematosus" is rejected because he felt it is "etymologically incorrect".

Haserick (1951) said that the term "systemic" should be used rather than "disseminated". He also felt that the commonly accepted classification of lupus erythematosus into acute, sub-acute and chronic types would seem to have become meaningless when patients, ill for several years, die from "acute" or "sub-acute" disseminated lupus erythematosus in the same way as those ill for weeks only. He felt that "disseminated" (literally, scattered) had as little significance as the term "lupus erythematosus" itself, applied to a patient with unblemished skin.

"Malignant" is a term, Haserick said, with significance only if the strictest definition of the word is adhered to, the adjective having been applied in lieu of "disseminated". The author feels that "malignant" is not the word of choice as its implication to him is of initiation and later spread, whereas this is not a known property of lupus erythematosus of the disseminated type. However, as with the term "leukoplakia", the author feels it would be useless to attempt to have discontinued the use of the term "lupus erythematosus", but that "systemic" seems a better word than "disseminated".

Haserick quoted Michelson, in a personal communication, saying that the disease should be graded according to a sum total of all factors involved in each particular case, in much the same way, it is felt, as was suggested in a different section of this paper, that "leukoplakia" (when meaning Hyperkeratosis complex) should be described.

Marten and Blackburn (1961) used a clinical classification which they said O'Leary had first used, the disease being divided into:-

1. Chronic discoid lupus erythematosus
2. Generalised (chronic) discoid erythematosus
3. Sub-acute disseminated lupus erythematosus
4. Acute disseminated lupus erythematosus.

In this classification, the author feels that they have denied the occurrence of a chronic disseminated form as had Rost and other writers earlier, but have apparently seen, from this writer's inference, a case of chronic discoid which has either exacerbated or was exacerbated (generalised) from the start. In a study of 57 cases of lupus erythematosus over a five (5) year period, they stated, however,

that no chronic discoid cases among the 57 cases of all types developed "systemic" lupus erythematosus, and only one case was transferred to the generalised discoid group. So that apparently the generalised discoid may develop from the chronic discoid or, by inference again, be "generalised" from inception. It would seem that a generalised discoid lupus erythematosus would not be as serious as the disseminated variety (primary); and as Wiener mentioned earlier, the chronic discoid type which exacerbates, in his opinion, systemically, may not, in the writer's opinion, actually become systemic at all, but rather become "generalised".

This would also tie in with Wiener's view that the chronic discoid which exacerbates is not as serious as the primary systemic type.

In their study, Marten and Blackburn concluded that, over the five (5) year period, those of their patients with the chronic discoid variety and with associated blood abnormalities were in no greater danger of developing systemic lupus erythematosus (if at all, it is felt) than those without blood abnormalities.

For the purposes of this review, a classification of:

1. Chronic discoid lupus erythematosus
- and 2. Systemic lupus erythematosus

will be used, with additional description if necessary (as suggested by Michelson).

4. Occurrence and Incidence.

In this review, prime consideration is to be given to those lesions of lupus erythematosus affecting the oral cavity as white lesions, but general occurrence of the disease must also be discussed at the same time.

Most authors, including Colby et al (1961), Shafer et al (1963), Bhaskar (1961), McCarthy and Shklar (1964) and others agreed that the chronic discoid form is relatively common. The mouth lesions in this form, however, are seen less commonly than the cutaneous lesions.

Bhaskar stated that oral lesions may precede, or follow, or be simultaneous with, the skin lesions and are seen in about 25 per cent of patients. In 1932, Greenbaum and Prinz had said that oral lesions were "commoner than formerly believed", 25 per cent of patients with cutaneous lesions also showing oral lesions. These latter, they felt, often escaped detection because they caused "little or no discomfort": the disease may be limited to mucous membranes, but it is rare to find no skin lesions. A year earlier, Monash (1931) had reported a 50 per cent occurrence of oral lesions in this chronic discoid type. Shafer, Hine and Levy gave a very non-committal figure of 25-50 per cent, whereas others, reported by Sugarman (1953), gave as their occurrence figure, under 30 per cent and Burket, under 20 per cent. In 1961, Marten and Blackburn found three (3) cases of oral lesions in 51 cases of chronic discoid type, less than 6 per cent. As in lichen planus, where both oral and cutaneous eruptions occur, difficulty can be experienced in determining percentage occurrence of oral against

cutaneous lesions, due to the presence or absence of either at the time of examination.

Monash pointed out that mouth lesions always followed skin lesions, but Lite (1953), and later Barnett (1961), were able to refute this statement, Barnett seeing a case of ultimately fatal lupus erythematosus which commenced on the gingivae, a case similar in initial site to that of Lite; cutaneous lesions appeared later.

Greenbaum and Prinz examined a case in which there was extensive oral involvement without cutaneous lesions at all.

McCarthy and Shklar stated that the chronic discoid type is rare in childhood and after the 6th decade. It usually occurs between the ages of 20 and 40 years, having a slight predilection for females, although Shafer, Hine and Levy feel it is far commoner in women than men.

The systemic forms of lupus erythematosus are seen less frequently, although Shafer, Hine and Levy felt that these types are increasing, but that this may be purely relative, due to more accurate diagnosis. The systemic type is nearly always found in young women between 20 and 40 years of age, according to all writers, the oral mucosa being a frequent area of involvement and in the opinion of McCarthy and Shklar, being particularly prominent as the disease reaches its fatal termination.

Orban and Wentz stated that nineteen (19) cases out of 104 cases of lupus erythematosus, presumably all types, examined at the Research and Educational Hospital of the University of Illinois (or about 20 per

cent) presented oral lesions.

It can be seen that much discrepancy exists in the figures given for occurrence of oral lesions in lupus erythematosus. The writer feels that the general statement that mucous membrane involvement in chronic discoid lupus erythematosus is seen less commonly than skin lesions is as dogmatic as is possible at present.

5. Aetiology

The cause is unknown. As stated in a previous section, it was once thought to be allied to tuberculosis, but there has been nothing to prove this, although the writer feels it is worth mentioning here that in Lite's case, reported in 1953, there was a history of tubercular infection, and the case was currently being watched for recurrent tubercular signs.

Keil (1933) concluded, after a study of the necropsies of 125 patients with lupus erythematosus, 25 of whom had tuberculosis, that the occurrence of tuberculosis in cases of lupus erythematosus is "coincidental and unrelated". He felt that the supposition that tuberculosis was bound up in the aetiology of lupus erythematosus would soon be discarded. At the present time, this is certainly true.

The collagen degeneration associated with this disease is assumed by some to be an allergic reaction to infection, particularly streptococcal (Orban and Wentz), one theory being that the infection may come from some focal area, such as the tonsils.

Both Lite, and later Barnett, mentioned the exacerbating (if not causative) effect of over-exposure to sunlight present in three (3)

cases they reported, Sugarman (1953) saying that sunlight causes relapse of skin lesions.

Much consideration is now being given to an "auto-immune" aetiology, which McCarthy and Shklar feel should be pursued as fully as possible.

"There exists enough evidence" said Damashek (1961), "to call systemic lupus erythematosus a complex auto-immune disease with an irregular involvement of various components of the blood vessels, resulting in a highly protean disorder; it possibly starts in one tissue and spreads to many." The author feels here that the "spread" would not necessarily be one that is similar to malignant spread, i.e. in cancer as is understood at present, i.e. a focal theory. It may be a "spread" due to one tissue being affected after another without necessarily being "focal" in origin i.e. coming from one initial focus.

The syndrome apparently occurs mainly in easily sensitised persons, in whom, for reasons at present obscure, groups of abnormal antibody-producing cells have developed and are forming abnormal antibodies continuously. As in a "graft-versus-host" reaction, the antibodies may attack the patient either at once (fulminating course - acute) or in an episodic fashion, gradually intensifying (progressive course - sub-acute or chronic).

Whether systemic lupus erythematosus may be said to be present at the appearance of the initial clinical symptoms, or whether the diagnosis can be made only in retrospect (after the development of a number of symptoms) should become clear with future studies.

At any rate, systemic lupus erythematosus has come a long way since it was thought to be a "toxic disturbance", to its present status of a complex auto-immune disease.

6. Clinical Manifestations.

Between the two clinical forms, there are numbers of intermediate manifestations.

Greenbaum and Prinz (1932) described the discoid type lesions on both skin and mucosa as progressing slowly, being more or less "fixed" - they are deep and infiltrated and such lesions of the chronic discoid type are the usual type seen. Cutaneous lesions are usually limited to the face and scalp, but new lesions may develop here and there, in a scattered manner, over the whole body.

In the diffuse type, the lesions are superficial and have a capricious course, tending to disappear and reappear, or to rapidly spread.

The intermediate types are variations and/or mixtures of the two types described.

Mucous Membrane Lesions: In the mouth, lesions begin as punctate bright red, ill-defined spots sometimes level with adjacent mucosa, - at other times slightly elevated, which, if joined together, form an irregularly shaped patch which soon presents a variable number of surface lesions partly covered with adherent, moist desquamations which are surrounded by dilated vessels. These vessels, "radiating" vessels according to McCarthy and Shklar, are a most striking feature. Later, the patch becomes slightly depressed at the centre, presenting a greyish-white atrophic area often surrounded by an erythematous edge.

Very old patches appear as sharply defined, whitish irregular scars which are slightly firm to the touch.

Greenbaum and Prinz, as stated previously, felt that subjective systems are conspicuous by their absence, except during acute exacerbations, and even then are generally not marked. In Barnett's two (2) cases, however, the oral lesions were painful. Greenbaum and Prinz also felt that tongue lesions were rare, appearing when present as irregular, painless, red, depapillated, non-infiltrated patches, which may be covered by hyperkeratotic epithelium: they are usually on the lateral margins, resembling "leukoplakia" (hyperkeratosis), scars from early syphilides, or lichen planus.

Shafer, Hine and Levy described the oral lesions of the discoid type as circumscribed, elevated white plaques, each with a red or purple periphery. Peripheral telangiectasis is also common as "picket fence" striae (Orban and Wentz). Erosion and ulceration of the mucosa frequently occur; red and superficial scarring may result, which is said by Archard et al (1963) to be the end result, after years, of recurrent ulcerations.

The buccal mucosa is usually most affected, intra-orally, followed by the lips, palate and tongue, which latter site is rarely involved, as previously stated. However, Hall (1943) reported a case in which there was only one area in the mouth involved and that was an area on the tongue. Any site in the mouth can be involved, said McCarthy and Shklar, adding that "the individual lesions may be difficult to diagnose, and offer a challenge to even the most experienced eye."

They and all others concur, that the mucous membrane lesions may appear alone, but that this is rare. Thoma and Goldman pointed out that oral lesions are most often found in the muco-buccal folds, usually bilaterally and symmetrically.

The course of the lesions may involve acute exacerbations and they may occur anywhere on the mouth, usually being localised, but may involve the entire buccal mucosa (Greenbaum and Prinz). They continued that oral lesions may be formed by direct extension from the face and/or lips: or they also agreed that they could be independent of any cutaneous eruption. Lesions were occasionally so typical in the mouth as to aid in clearing up an obscure skin diagnosis, they said. On the lips, lesions are dark red, sharply defined and irregularly shaped, with definite but slight infiltration. The lips can look "collodion painted" and the margins may show capillary dilatation. In chronic instances, the centre becomes atrophic and a definite greyish scar remains after healing, which may or may not be surrounded by a hyperaemic zone.

Sugarman (1953) stated that the lesions of the mouth enlarge by healing in the centre and breaking down at the periphery.

Oral lesions of the disseminated or systemic type are similar to those that occur in the discoid type except that they are more acute and more destructive. McCarthy and Shklar stated that they present a non-specific picture of bullae, erosions and necrotic slough. They are characterised by irregular ulcers of varying size and depth and have a telangiectatic tendency, being reddish-purple in colour.

Healing occurs centrally, with peripheral breakdown, and after healing the scar tissue usually is very easily traumatised. Oral lesions of the systemic type, however, are very variable and simulate many other diseases.

7. Skin Lesions

Greenbaum and Prinz (1932) described the cutaneous lesions as, characteristically, mildly to moderately inflamed, dark red or pink, more or less infiltrated macules or patches of irregular shape and size. They are superficial and covered in a more or less irregular manner with adherent greyish scales, forming an accumulation of varying thickness. These scales are peculiar, in that to their under-surface are attached small horny prolongations which fit into the follicular pores. The dilated pores are usually visible when the scales are removed. There may be one or several lesions: these lesions either slowly or rapidly increase in size by peripheral growth, or coalesce, when they can involve a considerable area. The patches are sharply defined against the sound skin by an elevated border, but as the lesions age, the centre becomes depressed and atrophic.

Archard et al stated that the skin lesions may be vesicular or bullous.

It seems that the lesions are most apt to appear on the face, the chest, the back and extremities, Greenbaum and Prinz stating that facial lesions appear especially over the bridge of the nose and the cheeks, on the ears, neck, scalp and the dorsum of the hands.

The discoid type forms, very often, the typical "butterfly" distribution on the malar regions and across the bridge of the nose,

but this is not always present, and as Shafer, Hine and Levy stated, it is not diagnostic, nor confined to this disease.

Orban and Wentz have noted a similar butterfly pattern on the palate, corresponding approximately to the distribution of the glands of the posterior portion of the palate.

In discoid lupus erythematosus, McCarthy and Shklar said that all patients whom they have examined with oral lesions have shown skin lesions.

The cutaneous lesions of the systemic type consist of erythematous patches, as in those of the discoid form. They also occur in the symmetrical butterfly pattern across the nose and face. These lesions may be pruritic or "burning" in sensation; they may be pigmented. The more acute, the more variable are the lesions, being at times even discoid in type, or just an erythema with some oedema. It seems that those areas exposed to sun (light) are the ones most prone to involvement.

McCarthy and Shklar said that the skin lesions may be entirely absent throughout the full course of the disease in the acute systemic type. It is felt that this could make clinical diagnosis very difficult.

8. The Systemic (Disseminated) Types of Lupus Erythematosus

Generalised Clinical Symptoms:

True chronic discoid lupus erythematosus has no systemic manifestations. Bhaskar stated that in "the acute form of disseminated lupus erythematosus", patients may have fever, pronounced leukopenia, hyperglobulinaemia, splenomegaly (which occurs, according to Pease (1956)

in more than 50 per cent of patients, also associated with lymphadenopathy), vomiting, diarrhoea, anorexia, dysphagia, vegetations on the heart valves (endocarditis) and fibrinoid degeneration of glomerular capillaries of the kidneys; or manifestations of any one, or group, of these symptoms. This latter condition of the kidneys is described as producing characteristic "wire loops", which can result in kidney failure (Shafer et al). Pease stated that constitutional symptoms occurring during acute phases of the disease, in addition to those mentioned, are weakness, fatigue, loss of weight and/or prostration. Arthralgias and joint symptoms are seen in some patients and it is difficult to distinguish between systemic lupus erythematosus and rheumatoid arthritis at times, without prolonged follow-up examination.

Pease agreed with Barnett, Lite and Sugarman and Stillerman (1960) that aggravating factors exist to exacerbate this disease. Pease mentioned focal infections, exposure to sunlight or severe cold, various allergic reactions and surgical procedures.

Lite and Barnett also found that there is sometimes a periodontal condition in which a looseness of some teeth can be demonstrated; selective grinding can alleviate this condition considerably.

Pease stated that involvement of the cardiovascular and central nervous systems is frequent.

Sugarman and Stillerman (1960) found that in a case which they followed for seven years, despite the smouldering course, the patient, a woman, progressed very well due to the fact that the disease did not attack a vital organ, such as the kidney. Yet L.E. factor tests were continuously positive.

Many case reports feature a "drawn-out" disease process, the more chronic in type being far better prognosis-wise, and these types can continue, with exacerbations and remissions, for many years.

Barnett summed up a case which he treated, by the terms "remission and relapse", which remissions and relapses did not always seem to be associated with the course of any superimposed disease, e.g. when the patient contracted pneumonia, the oral condition was sound and remained so until there was a sudden relapse about three (3) months later; but Barnett found it extraordinary that there was no extension of the area of oral involvement at any stage, though the tenderness increased. This is quite the opposite of Orban and Wentz's statement that there is always extension of the patches with each relapse.

An interesting point stated by Haserick is that patients can suffer from a generalised convulsion followed by a deep coma - epilepsy has been blamed for this, when no such condition as epilepsy exists for the particular patient.

9. Histopathology

Shafer, Hine and Levy spoke of the histologic appearance of all forms of lupus erythematosus as being similar, differing only in degree of certain findings.

The classic picture, according to McCarthy and Shklar, of the oral lesions of chronic discoid lupus erythematosus consists of a moderate parakeratosis or hyperkeratosis, hydropic degeneration of the stratum germinativum, degeneration of the connective tissue collagen and an infiltration of chronic inflammatory cells of a lymphocytic

nature, with also plasma cells and histiocytes, arranged in a perivascular pattern, which pattern can be obscured in heavy infiltration.

In skin lesions, the lymphocytic infiltration is seen in localised clusters which may or may not surround small blood vessels and skin appendages. The stratum germinativum of the epithelium presents areas of degeneration ranging from hydropic degeneration to complete cellular disintegration.

There is a hyaline-like degeneration of connective tissue collagen, both around the blood vessels and immediately under the stratum germinativum. P.A.S. staining for mucopolysaccharides shows intense reaction in the above areas of collagen degeneration, much more so than for lichen planus. McCarthy and Shklar felt that there is some doubt, in the skin lesions, of the presence of collagen degeneration in some workers' minds, but they themselves felt it is constantly present. This has been discussed in the "Introduction", but in order to enlarge on this a little, it is interesting to note that Bhaskar, Shafer et al, and Monash stated that the collagen degeneration here is basophilic in staining characteristics, while McCarthy and Shklar felt that it is lightly eosinophilic and Orban and Wentz that it is intensely eosinophilic.

McCarthy and Shklar concluded that the P.A.S. findings appear to be reasonably characteristic of chronic lupus erythematosus and have been noted in all cases studied by them.

In Acute Systemic (Disseminated) Lupus Erythematosus, fibrinoid degeneration of connective tissue is the characteristic lesion and is seen clearly in the various internal organs as well as the skin and mucous membranes. Both ground substance and degenerated collagen fibres may clump together into amorphous eosinophilic sections. There is lymphocytic invasion of the perivascular type with, again, plasma cells and histiocytes. An interesting, possibly diagnostic, specific structure, according to McCarthy and Shklar, may be found in the lesions of visceral organs. This is termed a haemotoxilin body, and is probably composed of nuclear D.N.A. material.

Both skin and mucosa present extensive hydropic degeneration of the stratum germinativum of the epithelium and there may be some epithelial atrophy and spongiosis.

Lesions of the oral mucosa, especially of the gingivae, demonstrate greater inflammatory infiltration than skin lesions and may also present non-specific ulceration in areas, rendering a microscopic diagnosis more difficult.

General Histopathology: Orban and Wentz stated that biopsies taken from older lesions, which are white and raised show hyperkeratosis and hyalinisation of the connective tissue. They also mentioned the appearance of peculiar keratotic plug formation in the epithelium with lamellated horny layers, giving the lesion the white appearance of scarred areas seen in the cheek or palate. This has been mentioned before in the section "Clinical Manifestations". In these cases, they said that the connective tissue is free of inflammatory cells. Large epithelial horny pearl formations can be seen in an "onion-ring"

pattern, which formations indicate a disturbance in the normal maturation process of the epithelial cells.

Shafer, Hine and Levy felt that not all features are invariably present in each case. They, and Archard et al found the same, noticed the lack, in some cases, of rete pegs which, when present, were atrophied. They also noted the inflammatory infiltrate "surround" of skin appendages. Sugarman pointed out the marked oedema usually present and the dilatation of the blood vessels, adding that hypertrophy may not always be present in the epithelium; at times, the condition was an atrophy of epithelium. McCreight and Montgomery (1950) also found oedema of vessel walls, stating that it was a most notable feature, but finding "little evidence of fibrinoid degeneration of collagen". They gave the results of a histologic study of 119 specimens from cutaneous lesions of lupus erythematosus, 102 from systemic lupus erythematosus and 17 from the chronic discoid variety. They found the histologic changes to be similar in all the various types, but the change was in degree dependent, it seemed, on the age of the individual lesion. They concluded that distinction of the disease based entirely on histologic evidence was "impossible".

10. Diagnosis.

Chronic Discoid Lupus Erythematosus

Bhaskar stated that, in the absence of skin lesions, and with only oral lesions manifesting, a clinical diagnosis of acute or chronic lupus erythematosus would be impossible and, under similar conditions McCarthy and Shklar felt it would be extremely difficult to make a

definite statement of diagnosis. In the case reported by Lite, a diagnosis was not made until the cutaneous lesions appeared and Sugarman stressed that diagnosis by oral lesions alone should never be attempted. Clinically, however, as stated previously, oral lesions may occur alone, especially in the systemic form.

According to most writers, the presence of the radial arrangement of capillaries can be helpful, the general concensus of opinion being that histological examination is only an aid, although P.A.S. stain results could be of great help. But the author feels that the presence of (concurrent especially) skin lesions is the most helpful feature in diagnosis.

The Systemic Type Lupus Erythematosus

The age and sex of the patient in the clinical diagnosis of systemic lupus erythematosus is important, and Shklar and McCarthy felt that any young female presenting with vague symptoms of fatigue, low grade fever, a skin rash and joint soreness should be suspected. "Suspicious, atypical lesions" said Lite, "require constant observation and thorough investigation, even where treatment has been instituted. Local treatment may seem to modify the effects of systemic disease and produce a pseudo-cure which may be misinterpreted in view of the final results".

Leukopenia, anaemia and increased blood sedimentation rate are common. Urinalysis may reveal protein and cells.

The most important diagnostic aid is the lupus erythematosus phenomenon, which is a test, the L.E. factor test, as originally

demonstrated by Hargraves and refined by Haserick. The test consists essentially in the addition of the blood serum, from a person under suspicion, to the buffy coat of normal blood. If the patient is suffering from acute disseminated lupus erythematosus, typical "L.E." cells will develop, or, if not then, at some time during the course of the systemic disease. This "L.E." cell or phenomenon consists of a rosette of neutrophils about a pale nuclear mass apparently derived from a lymphocyte. The L.E. phenomenon, however, can be seen sometimes, said Bhaskar, in rheumatoid arthritis, leukaemia and multiple myeloma. Haserick had noticed this and felt that the plasma L.E. test either:

1. Gave false positive results
- or
2. that acute systemic lupus erythematosus is actually a frequent protean disease with atypical phases which may be detected with certainty by the plasma L.E. Test.

In other words, rheumatoid arthritis (as diagnosed!), leukaemia, etc. were just manifestations of systemic lupus erythematosus.

N.B. The L.E. test was positive in all patients with acute systemic lupus erythematosus. However, the author feels that the phenomenon may not necessarily be specific for lupus erythematosus: it was positive, as pointed out in the "Introduction", in penicillin allergy and in Hydrallazine therapy. Could it be a general test for all hypersensitivity reactions or even conditions not classed as hypersensitivity states? However, there is no evidence for this as yet.

When human marrow was used as the indicator, the number of L.E.

cells was employed also in "rating" the degree of positivity of the test. The higher the number of clumped leucocytes (or L.E. cells), the more convincingly positive the test was considered. As the disease condition improved or went into remission, so the number of cells diminished.

In one acute case of the disease, a negative L.E. test resulted. Haserick et al credited this to the loss of gamma globulin in the urine and thus a low gamma globulin level seemed at first to be the most credible explanation for a negative L.E. test. They felt the L.E. test may prove of great value in providing a means for better understanding of the problem of lupus erythematosus, especially the problem of grading just mentioned. It may help, too, in differentiating diseases, thought to be rheumatoid arthritis, but which are atypical. Some cases of supposed rheumatoid arthritis have actually turned out to be lupus erythematosus and this may be the reason why positive L.E. tests in rheumatoid arthritis, in cirrhosis or even multiple myeloma may be found: as previously implied, the particular conditions could have been wrongly diagnosed.

A high gamma globulin content does not necessarily mean a positive test, as there were cases in which the L.E. test was negative, yet a high gamma globulin level was noted. Apparently though, low gamma globulin can lead to a false negative result.

Weiss and Swift (1955) stated that "all cases of rheumatoid arthritis should have frequent L.E. tests performed, especially if they show even minimal symptoms referable to lupus erythematosus. Particularly is this true if they have mild bouts of fever, accompanied by pain and

by reversal of the albumin-globulin ratio with markedly increased globulin, microscopic evidence of kidney involvement and increased sedimentation rate."

The fact that one or two "cells" have been found in the blood of patients who do not seem to be ill, coupled with the fact that the hydrallazine syndrome seems to be so readily reversible, makes one think that perhaps the concept of lupus erythematosus as an invariably fatal disease should be modified. Hitherto, diagnoses could only be made when the disease was severe (and "irreversible?"). Perhaps some persons experience a mild, sub-clinical attack of systemic lupus erythematosus from which they recover, or perhaps some cases manifest as rheumatoid arthritis or related syndromes.

In theory this sounds very well, and may prove to be true. However, the writer also feels, whereas in experiment the L.E. phenomenon is reversible by withdrawing a causative agent, in actual fact, once the disease process is commenced, it could well be that it is irreversible from the very start.

Up till the L.E. factor test was used, systemic cases of lupus erythematosus could well be misdiagnosed. A case presented in 1942 by Feigenbaum is one in point, seeming from all the clinical symptoms to be systemic lupus erythematosus. However, therapy of the accepted type failed to produce any remission. While this case was not necessarily misdiagnosed, it would have been very acceptable to have the confirmation or denial of an L.E. test.

11. Differential Diagnosis.

Other conditions may resemble the oral hyperkeratotic lesions of chronic discoid lupus erythematosus, or the vesicular and erosive oral lesions of systemic lupus erythematosus.

Chronic Discoid Lupus Erythematosus:

(a) Lichen Planus: Monash said that lichen planus is usually bilateral, on the buccal mucosa opposite the molar teeth. It is characterised by its whitish striae and a violaceous hue, in a lace-like effect. It seldom has accompanying inflammatory reactions. It also usually has characteristic skin lesions. McCarthy and Shklar said that no difficulty would be experienced in differential diagnosis in the classical forms of lichen planus. They felt it is also more extensive than chronic discoid lupus erythematosus. Histologically, the only real difference is the inflammatory response in which lichen planus exhibits an infiltrate which "hugs" the basement membrane, or perhaps the appearance of the collagen degeneration in lupus erythematosus.

(b) Keratoses)
Hyperkeratoses): These conditions are usually found in elderly men and, histological evidence is very helpful (Monash). McCarthy and Shklar advised that the appearance in lupus erythematosus of the typical peripheral vascular arrangement should decide the issue. They also felt that in the case of lupus erythematosus, "the location is often in a site free from possible mechanical irritation" - the author feels it would be dangerous to eliminate the hyperkeratoses on these grounds. In Barnett's two (2) reported cases, some affected areas in the mouth resembled leukoplakia.

Systemic Lupus Erythematosus, (Acute)

(a) Benign Mucous Membrane Pemphigus: The patient suffering from the above disease would be free of constitutional symptoms, while a patient with systemic lupus erythematosus, would be ill. In cases of chronic discoid type showing erosions, there is still an area of peripheral tissue and vascular change which is not present in pemphigoid. McCarthy and Shklar stated that pemphigoid nearly always involves the gingiva, but much reliance on this, it is felt, would not be wise.

(b) Syphilis: Monash stated that mucous patches can resemble lupus erythematosus in that they are usually bilateral. However, their site of predilection is the tonsillar area, where lupus erythematosus is rarely seen. However, the point that this writer would raise is that again this would be a very flimsy piece of evidence on which to rely alone. Syphilitic patches are also surrounded by less inflammation than the lupus erythematosus patches. McCarthy and Shklar have relied on serologic tests for syphilis. One cannot rely on a classical syphilis pattern of split papules at the mouth corners, accompanying the angular mucous patches. Monash said that the peculiar whitish lines and bright red colour of the lesions of systemic lupus erythematosus would not be present in syphilis, although the author feels syphilis could imitate these type lesions very well.

12. Therapy

In 1932, Greenbaum and Prinz, using intravenous injections of gold-sodium thiosulphate, had achieved, they said, remarkably successful results in the treatment of lupus erythematosus, having used, previously, local treatment with iodine and sodium perborate or carbon

"C" light rays without success. Iron and arsenic had been administered internally with little benefit. They felt the remarkable improvement following intravenous injections of gold-sodium thiosulphate was practically corroborative of the diagnosis.

In Lite's case, over twenty years later, systemic treatment with intravenous gold-sodium thiosulphate was used and the lesions were responding, when an allergy to gold salts developed, necessitating a change to a bismuth salt.

Monash (1931) had injected gold-sodium thiosulphate directly into the lesions, later followed, if necessary, by electrocoagulation to completely destroy them. In addition, he required abstinence from any locally applied irritant, such as smoking. The obvious disadvantages of this method were replaced by intravenous therapy.

The heavy metals, gold, arsenic, bismuth, etc., are condemned now by McCarthy and Shklar. They feel that their use was followed by doubtful benefit; "cures" were possibly spontaneous.

As stated before, both Lite, and later Barnett, noted periodontal conditions associated with lupus erythematosus. To eliminate looseness in the teeth of his patients and so to aid the periodontal condition, Lite had adjusted the bite, which resulted in a much more comfortable mouth, especially when 10 per cent benzocaine ointment was prescribed, to permit massage of the gums without pain in the ulcerated areas. This aided formation of keratin and after about one year, remarkable improvement had taken place; Barnett's course of therapy was much the same, with similar good results. However, Lite stressed that localised treatment will not eliminate, but may reduce, the effects

in the mouth lesions of this systemic disease, warning that treatment of the local lesions alone, rather than the disease, may merely serve to delay proper and essential treatment.

Strean (1957) felt that the oral lesions of the chronic discoid type may be treated with hydrocortisone acetate dental ointment (2.5 per cent).

In lupus erythematosus with a slowly progressive course over many years, accompanied by spontaneous exacerbations and remissions, Barnett stressed that patients with, say, teeth to be removed due to infection, usually have an exacerbation after the necessary surgical procedure in removal - he recommended the prophylactic use of an antibiotic, together with a course of cortisone therapy. Barnett found that, in systemic lupus erythematosus, cortisone and adrenocorticotrophine were not effective in one case which he reported, although there had been much hope held out for its effectiveness (Strean, 1957).

Sugarman pointed out that both cortisone and A.C.T.H., although producing, clinically, striking results, do not effect a cure of the underlying disease process, as proved at post-mortem at which time treated patients had no different lesions histopathologically from untreated ones. It seemed to Sugarman that lesions should be treated indefinitely or until possible spontaneous remission occurred, but that there were great hazards involved, because of the side effects induced. McCarthy and Shklar pointed out the usefulness of cortisone and allied drugs in crises of the disease.

Sugarman and Stillerman felt that the steroids are the drugs of choice in the systemic form, despite possible side effects. They felt,

like Barnett, that as patients were prone to secondary infections, antibiotics could also be used in conjunction. They stated, however, that this use could lead to conditions such as moniliasis. However, in a case reported by them, Herpes Zoster Ophthalmia developed which they described as "coincidental". The author feels that such may not be the case, as there could be some predisposing factor possibly induced by therapy. After seven (7) years of therapy in the above case, they concluded that "it is still impossible to state the duration of life expectancy of this patient".

Orban and Wentz have warned that the use of drugs such as predisone, though potent, suppressive agents, may bring on the acute form if used against the chronic discoid type. The writer feels this is very important.

Marten and Blackburn used chloroquine, 200 mg. b.d. for treating patients with lupus erythematosus; they also used mepacrine, 100 mg. b.d. for others. They noted no side effects. McCarthy and Shklar have reported that these anti-malarial drugs, as used by Marten and Blackburn, have made a significant advance in the treatment of the chronic discoid type, stating that few sufferers are not helped by the use of these drugs, with skin lesions responding better than the oral ones. They do stress, however, that the disease is again being controlled, not cured. Whereas side effects are not common, blood forming tissues may be suppressed and gastro-intestinal or visual upsets may be produced; Retinal degeneration has been observed, resulting in possible blindness. They therefore caution the

employment of the anti-malarial drugs, recommending their use only when the condition is serious.

Barnett used chloroquine, an anti-malarial, with good "suppressive" or "control" results - the drug seemed to keep the condition in check, but it still progressed. Atabrine is recommended by Urban and Wentz, 0.1 gm. b.i.d. for two weeks, after which 0.1 gm is taken daily thereafter for up to a year. Chloroquine is the drug of choice for control of the chronic discoid type by McCarthy and Shklar, in doses of 250 to 750 mgms. daily. They said a drug combining atabrine, primaquine and chloroquine, in one tablet, is also available. They stressed also, despite the warnings of possible harm caused by the drugs in therapy, that if the disease is left untreated, scarring will occur. Honig (1956) described methods of plastic repair to noses, cheeks and lips disfigured by the cutaneous lesions; a dread thought, and the clinician must decide very carefully before decisions as to therapy are made; will he risk possible later disfigurement to his patient or the possible side effects of his therapeutic drug?

C. LICHEN PLANUS (Lichen Ruber Planus)

1. Definition

This disease is an inflammatory one, involving both skin and mucous membrane in keratotic lesions of varied pattern. Shafer, Hine and Levy (1963) stated: "Lichen planus is of considerable interest to the dentist because involvement of the oral mucous membranes commonly precedes the appearance of lesions on the skin. It is one of the most

common dermatologic diseases to manifest itself in the oral cavity --."

All modern texts agree that oral lesions may occur alone, or they may precede, accompany or follow cutaneous lesions.

2. Introduction:

Erasmus Wilson first described the disease in 1869 as Leichen Planus and in 1885, Thibierge first set down a description of the oral lesions in a systematic way, stating as in McCarthy and Shklar (1964) that "in most cases the lesions occurred on the buccal mucosa and the tongue, with certain differences in appearance. On the tongue, the eruption was described as white spots, round or slightly irregular in form and without notable prominence. The lingual papillae appeared diminished in depth. The spots might be isolated or joined and in some cases they formed parallel lines at the border of the tongue. On the buccal mucosa, the lesions were usually numerous, small papules, rounded or stellate in shape, pure white and often shiny. The papules were isolated, formed plaques, or interlacing, diversely placed lines. Between papules, the mucosa presented superficial ulceration. Although the plaques could cover the entire buccal surface, they were usually localised to the area of the molar teeth. In the rest of the mouth, the papules were isolated or in small numbers."

Unna, in 1882, had also described oral lesions and believed that they were an occasional accompaniment to the generalised skin eruption, but Audry, in 1894, noted that they could occur without any cutaneous signs whatsoever. In 1906 Dubreuilh stated that mostly skin and oral

eruptions were found together, but that oral lesions alone were more common than involvement of the skin without oral lesions and also noted the identical picture presented histologically by both cutaneous and mucosal lesions. He suggested oral biopsy as a diagnostic aid, mentioning the cellular infiltration of lymphocytes in the immediate sub-epithelial connective tissue, rarely accompanied by plasma cells and polymorphs; the epithelium itself, he noted, showed only some oedema and slight hyperplasia.

So by this time a fairly accurate description of the disease had been presented.

3. Occurrence

According to Shklar and McCarthy (1961) most cases of lichen planus have both oral and dermal lesions, yet Cooke (1954) noted only three (3) of 50 patients in his survey with accompanying skin lesions. Robinson (1954) stated that the disease is found in the mouth more frequently without, than with, skin lesions. Bhaskar (1961) felt, however, that 50 per cent of all patients with lichen planus show oral lesions, which may precede or follow the cutaneous ones. In a study of 58 patients with skin lesions, Orban and Wentz (1960) noted oral lesions were present in 21; but could be confined to the oral cavity in 10 per cent of cases. Oral involvement has been described as being as high as 50 per cent, according to Burket (1961), a similar percentage to that of Bhaskar. In some of the older surveys noted, a figure of 10 per cent for lesions confined to the oral cavity was given, agreeing with the percentage given later by Orban and Wentz.

The author feels that these figures only have value at the time of examination, relying as they do on the site of the lesions at examination time and also on information given by the patient as to any previous site. Oral lesions seem to appear long before those on the skin. It is felt that, in follow-up cases where previously only the mouth had been involved, cutaneous lesions could appear later or even other mucous membrane involvement become apparent, such as the penis, vagina or epiglottis. Of course, any of these sites could be involved independently of, or concomitant with, skin and/or oral lesions.

Dechaume and Payen (1961) considered isolated oral lichen planus "as a form of leukoplakia - which occasionally exhibits a tendency to fissure and, later, to malignant change". This "malignancy" will be discussed later. They said that in this particular type of lichen planus, the lesions seldom appear on the cheek, tongue, or lips and stated how important this is as the "diagnostic" difference between the disease and leukoplakia buccalis.

Shklar and McCarthy (1961) set down the following data on the location of the oral manifestations and incidence of occurrence:-

On the buccal mucosa -	80 per cent,
On the tongue	- 65 per cent,
On the lips	- 20 per cent,
On the gums, palate and floor of the mouth	- less than 10 per cent.

Both sexes seemed to be equally involved and the ages of affected persons ranged from thirteen (13) to seventy eight (78) years. However,

most text books stated that children are rarely affected and Shafer et al felt that women are somewhat more affected than men.

4. Clinical Features.

The lesions of lichen planus are basically small, hemispherically raised papules. The oral papules (or lichens) produce, usually, glistening white to greyish-white lesions, except on the tongue, where they do not glisten and tend, each papule, to be more flattened.

The overall appearance of oral lesions depends upon the way in which the papules may coalesce and arrange themselves, so that thread-like lines, which are usually slightly raised, are often seen intersecting one another, white dots being frequently present at the crossing of the lines or "striae", these striae being named after Wickham, who first described them in 1895. The striae may be arranged in a linear, reticular or circular pattern and the occurrence of some lesions in a linear fashion is said to be associated with the course of a nerve (Darling and Crabb, 1954). At times, many papules abut together in one mass, forming plaques and losing macroscopically their individuality. If not quite coalescing they may form a papular pattern, which is similar to a plaque lesion, but allows the papules to retain this individuality. Sometimes, an annular pattern is observed. Shafer, Hine and Levy (1963) felt that the classical pattern is one of "Lesions consisting of a series of radiating white or grey, velvety, thread-like criss-crossings in a reticular pattern, most commonly seen bilaterally on the buccal mucosa".

Cooke (1954) mentioned lesions of the soft palate which appear in a pigmented pattern.

The author would stress the importance of an "overall" examination of the oral cavity in any case presenting for diagnosis. In three cases of ulcerated lesions described by Darling and Crabb (1955), the ulcerations were the focal point of attention in the examination, and if associated papules or striations of lichen planus were not noted, a false diagnosis could be made. This ulceration can persist, with remissions, for many years and they considered it a type of chronic, gross ulceration different from any previously described in association with lichen planus.

As shown before, the buccal mucosa is the site chiefly involved in lichen planus of the mouth, mostly bilaterally. McCarthy and Shklar (1964) felt the involvement is 85 per cent, which is greater than their assessment of 1961 - (80 per cent). If small enough, the manifestations, usually of the reticular pattern, are at the level of the occlusal line. Orban and Wentz (1960) said that the lacy or reticular pattern is on a reddened, inflamed background. If the cheek is involved in a punctate linear pattern, individual papules may appear as a series of white dots on a violaceous background and the dots form lines roughly parallel to the occlusal line. The plaque and/or papular patterns may also be present, often in conjunction with any other type pattern or patterns. But as Colby, Kerr and Robinson (1961) stated, always, in diagnosis, look for some evidence of the classical Wickham's striae, as they often occur at the periphery of less common type lesions, such as the plaque.

Vesicle and/or bullae formation (s) can occur in lichen planus -

they are rare, (Shafer et al, 1963; Colby et al, 1961; Orban and Wentz, 1960 and McCarthy and Shklar, 1964). If this type of lesion is found in the buccal mucosa, say, ulceration can occur either related to trauma or local irritation. The ulcerated or erosive type, however, usually begins as such and "not as a progressive lesion of initially non-erosive lichen planus" (Shafer et al). So that this vesicular type of lichen planus can be mistaken for the erosive form if ulceration or erosion has taken place.

The author feels that, while these signs of vesicle formation and/or ulceration are important, they are just manifestations of the different courses one disease may take according to circumstances of environment, both local and general, idiosyncrasies of tissue composition, tissue reaction, etc.

Kutscher and Zegarelli (1957) stated that it is possible, in patients with erosive type lichen planus, to discern some patches of non-erosive type; so that the clinical appearance should not be completely masked.

The tongue is second in degree of involvement and lesions there may differ from those of the buccal mucosa and also vary considerably in themselves. The reticular pattern is typical, usually occurring on the lateral borders and bilaterally. The dorsum may be involved, sometimes entirely, or may be completely lesion free. The lingual papillae become atrophic in both involved and uninvolved areas and the resulting smoothness accentuates the striae. The papules can form circles and rings; Orban and Wentz felt that these round, or annular, lesions are the most characteristic of the tongue lesions - due to the

presence of the atrophic lingual papillae, the centres of these rings are reddish and smooth. This type of atrophic glossitis, with or without the white lesions, is very similar to the atrophic glossitis of tertiary syphilis, to which it is entirely unrelated. Only biopsy and serological studies will offer a definitive diagnosis. It has been noticed that this form of lichen planus tends to occur in elderly females.

Colby et al showed a tongue dorsum with an area resembling keratosis and said that sometimes this involvement has a verrucous appearance. While uncommon (McCarthy and Shklar), it can occur where there is wider involvement, as in this case. The vesicular form may also appear and this may lead to ulceration through irritation, or the ulcerated (erosive) pattern may be present from the start.

The author emphasises again the importance of looking for the white lines and papules of the "typical" lesions, often found adjacent to any "atypical" (so-called) area.

The vesicular type, if it forms at all, usually does so on the lateral borders, but can present on the ventrum. The lesions may be bullous in character, sometimes even fluctuant and are whitish with a violaceous hue. If rupture of a bulla should occur, the covering is seen to be very thick, because the full depth of the epithelium is raised; this will be explained in the following histopathology. The vesicular fluid is mostly clear but, if infected, may be haemorrhagic or purulent.

Plaque pattern may be seen on the tongue and as the lingual papillae are atrophied, may not appear raised as usual, sometimes even

appearing slightly sunken. Plaque distribution over the tongue surface may be patchy in character.

The Lips are rarely involved in lichen planus, but if involvement should occur, it is usually the lower, at times involvement being confined to this area alone. The type is usually of the annular, reticular or plaque form, being rarely vesicular or erosive. Where lip lesions exist alone, diagnosis can be difficult. The floor of the mouth may be involved, but rarely. The hard palate can also be affected (Shafer et al, Bhaskar), as well as the gingivae, the latter being uncommon (Colby et al). Lesions affecting the gingivae have been described as usually "milky white patches" (plaques) - (Orban and Wentz) - or reticulated (McCarthy and Shklar). The gingival margin is usually free of involvement.

Some writers (Ziskin and Silvers, 1945) described an erosive type of manifestation involving the gingivae and some (Colby et al) mentioned the care that is needed in the differentiation between this erosive lichen planus and desquamative gingivitis. However, McCarthy and Shklar feel that desquamative gingivitis is a non-specific gingival manifestation of a variety of systemic disturbances and that it is not particularly surprising to find desquamative gingivitis associated with lichen planus. So that these authorities consider the erosive lesions of lichen planus on the gingivae to be really a desquamative gingivitis brought about as a result of the lichen planus per se and/or possibly the causative agent of the disease.

The author sees no reason to differentiate between erosion on the gingivae and erosion on any other involved oral region during the

course of the disease, where it is of the idiopathic erosive type from the outset.

5. The Skin Lesions of lichen planus are quite distinctive and usually can be diagnosed readily. The eruption is mostly pruritic or itchy and begins with the small, roundish, flat-topped papules, about pin-head size to one or two millimetres in diameter, which often coalesce into larger plaques, having a scaly glistening surface. The papules are sharply demarcated from their surrounds and the lesions appear reddish-brown at first. When well developed they take on a violaceous hue. When healed, the sites remain as brown macules mostly, due to the presence in the upper dermis of numerous melanophores. Pigmentation, after healing, in the oral cavity is very rare, although Cooke, as mentioned earlier, did notice pigmentation in lesions of the soft palate (McCarthy and Shklar).

The flexor surfaces of the arms and legs, old scars (Orban and Wentz), the sacral region and the external genitalia are the most common cutaneous sites, but the lesions can occur anywhere on the skin surface. The face, according to Shafer, Hine and Levy, is usually not involved. Nail beds can be affected (Darling and Crabb, 1954) although this is rare, and papules can be seen through the nail, which is grooved and ridged.

6. Symptoms

Most authors agree that oral lesions lack symptoms of any kind, as distinct from the pruritis of the skin lesions, although there may be glossodynia or glossopyrosis. Lesions are discovered in the mouth during visual examination but if the lesions are bullous or erosive,

patients may suffer severe pain and are as uncomfortable as in other diseases featuring bullae or erosions, such as pemphigus or erythema multiforme.

7. Aetiology

The aetiology is not known, but seems to be associated with emotional tension. The following causes have been advanced over the years - (McCarthy and Shklar) - (Cawley and Kerr, 1952):-

1. Traumatic
2. Specific Bacterial
3. Syphilitic
4. Parasitic
5. Viral
6. Mycotic
7. Allergic
8. Toxic
9. Neuregenic
10. Hereditary
11. Psychosomatic
12. Malnutrition.

Factors contributing to the cause have been given as smoking, mouth irritation and overwork.

Jacob and Helmbold claimed to have isolated a specific bacterial agent from the lichen planus lesion, an anaerobic, gram negative bacillus, but this has not been proven. Sunlight has been said to cause recurrence of lip and skin lesions (Darling and Crabb, 1955).

Such a great amount of evidence seems to point to lichen planus being associated with some form of emotional trauma, that there surely must be some link with it. Warburg (1956), in discussing aetiology of disease, stresses the importance of real or basic cause - it follows that emotional disturbance or stress could predispose to this condition, the gate thus being opened to some "actual" causative agent. It has been stated that, occasionally, a particular emotional upset may be "over"

some time before the disease manifests itself: the author agrees. Examinations, failure in career, the death of a loved one, may precipitate the condition: however, rarely is it noticed in the psychotic or the carefree. McCarthy and Shklar concluded that psychiatric evaluation of the patients with lichen planus could reveal "significant information".

A case, however, reported by Kresburg and Douglas (1956), was unusual in that the patient was a young, healthy male, not the nervous type, had no particular worry, was a teetotaler and a non-smoker.

Warin, Crabb and Darling (1958), in an excellent article on the disease, stressed a psychosomatic cause, and the author does not feel that the case reported by Kresburg and Douglas necessarily refutes this opinion, without the psychiatric evaluation of the patient as recommended by McCarthy and Shklar.

It is interesting to note here that the use of atabrine has produced lesions identical to lichen planus both clinically and microscopically: it may be that the lesions are actually those of lichen planus. Goldberg, as reported by Darling and Crabb (1955), said that cases could be cured even with the continuation of atabrine therapy. However, it is felt that this would not necessarily rule out atabrine as an "initiator" of the disease.

8. Course

The disease is considered chronic, although Pindberg (1959) stated that it may appear in an acute or chronic form. Darling and Crabb (1954) confirmed this and felt that, in the acute form, lesions of the oral mucosa are relatively rare, while skin lesions develop at

great speed, most of the body surface being covered: this form can develop in 24 to 48 hours and the patient may be very ill indeed.

In the chronic form, there are frequent periods of remission followed by exacerbation, often corresponding to emotional stress. Several months to a year or more is typical of its course: it may spontaneously disappear.

9. Histopathology

The appearance under the microscope is quite characteristic, Shafer, Hine and Levy calling it pathognomonic. Most authors agreed that the classical histopathologic features of lichen planus in the mouth are parakeratosis, occasionally some acanthosis with intra-cellular oedema of the spinous cells, some downward extension of the rete pegs giving them the appearance of the teeth of a saw, hydropic degeneration of the stratum germinativum (basal cell layer) and finally, infiltration of lymphocytes and only occasional plasma cells into the sub-epithelial layer of connective tissue immediately beneath the basal cell layer, the deeper submucosa being free of chronic inflammatory cells. This absence of plasma cells in the subjacent connective tissue is stressed by Orban and Wentz as an important diagnostic feature. They favoured a hyperkeratotic condition, with an increase in the granular layer, rather than parakeratosis (which hyper- or para-keratotic condition explains the white appearance of oral lichen planus lesions). McCarthy and Shklar, in mentioning the "saw tooth" appearance of rete pegs in the disease, noticed that, whereas this feature is typical of skin lesions, it is not necessarily so in the case of oral ones. They agreed with Colby et al, that the rete pegs may be generally flattened,

such as in the atrophic type where covering epithelium is thin and the rete pegs flattened.

"True dyskeratosis does not occur" stated Shafer, Hine and Levy; and others, including Shklar and McCarthy (1961), concurred, although Orban and Wentz, conceding that a precancerous state is not generally attributed to lichen planus, indicated that isolated oral lesions, without accompanying skin lesions, may become malignant. The liquefaction degeneration of the basal cell layer may involve just one small section here and there, or the layer in its entirety, the process extending at times up into the stratum spinosum, with accentuation of the protoplasmic inter-cellular bridges. McCarthy and Shklar stressed that this hydropic degeneration may be only slight, leaving the general appearance of the basal layer as normal. At times, eosinophilic clumps of hyaline degeneration may appear in the corium and lower epithelium. They said that the more the epithelium degenerates, the more it seems to be infiltrated by inflammatory cells, owing to the so-called liquefaction of the basement membrane. If this membrane is apparently normal in architecture, the lymphocytic inflammation may appear to be separated by a narrow zone of connective tissue.

P.A.S. staining for mucopolysaccharides reveals a well-stained inflammatory zone and underlying connective tissue, and a thin basement membrane sharply defined. The epithelial cells are mostly free of mucopolysaccharides, but parakeratosis stains deeply.

In bullous and vesicular lichen planus, the area of hydropic degeneration undergoes further disintegration and fluid filled spaces may result at the connective tissue-epithelium junction, the epithelium

being lifted up as more fluid is formed, vesicles or bullae being produced according to the amount of fluid liberated. There may often be lymphocytes, polymorphs and histiocytes seen in the fluid spaces. Shafer et al felt that there may be a weakness between epithelium and corium in cases of lichen planus, as an artefactual tearing is so often seen at this junction on microscopic examination and they stated this could be an aid in diagnosis.

The use of the description "pathognomonic" with regard to the histopathology is not justified, in the author's opinion. Clinical evidence, such as the appearance, distribution and course of the lesions should be considered. Certainly the microscopic appearance can be strongly suggestive of lichen planus, although at times in the early stages, the picture is one of non-specific chronic inflammation, later becoming more differentiated in the majority of cases.

It would seem that the classical clinical appearance would not necessarily require biopsy, but the author would not hesitate to use it if any doubt existed whatsoever.

10. Differential Diagnosis

It would be well to re-state here the "key" symptoms and signs of lichen planus:-

1. Primary small papules; in turn coalescing to form the several possible types of variation.
2. The chronicity (usually)
3. The presence or history of skin lesions which are usually itchy.
4. The symptomless oral lesions, unless they are bullous or erosive.

Biopsy should be employed in difficult cases.

Oral lesions bearing a resemblance to lichen planus include chronic discoid lupus erythematosus, benign mucous membrane pemphigoid, pemphigus vulgaris, erythema multiforme, syphilitic mucous patches, moniliasis and the hyperkeratoses.

(a) Chronic Discoid Lupus Erythematosus can present plaque type lesions, confined to the oral mucosa. The microscope is often of considerable assistance in the diagnosis here, as chronic discoid lupus erythematosus presents a parakeratosis, some hydropic degeneration of the basal cell layer and degeneration of the connective tissue collagen. However, the inflammatory cells (lymphocytes) of the corium are perivascular in distribution, unlike the subjacent lymphocytic infiltration of lichen planus.

(b) Pemphigus: Benign mucous membrane pemphigus (pemphigoid) and pemphigus vulgaris may resemble erosive or bullous lichen planus, benign mucous membrane pemphigus being chronic and lacking constitutional manifestations, but involving the conjunctiva, whereas lichen planus does not, nor does pemphigoid have "infiltrative" lesions (lateral spread).

Pemphigus vulgaris, microscopically, has acantholysis with the formation of intra-epithelial vesicles (Cooke, 1960), not junctional vesicles as in lichen planus.

(c) Erythema Multiforme's acute nature tends to eliminate this disease, as well as the usual severe involvement of the labial mucosa.

(d) Hyperkeratosis may resemble the plaque form of lichen planus, but is best diagnosed by a biopsy. Most authors agree that lichen

planus is not associated with malignant change, but there have been quoted a number of instances of carcinoma in the mucosal lesions of lichen planus - it is felt here, however, that as lichen planus is a chronic disease, there could be a "superimposition" of the malignant condition over a period of time due to a number of factors, not the least of which could be frictional irritation: thus, lichen planus may not be possessed of potentially malignant oral lesions per se, but the mucous membrane affected by lichen planus may, in some way, be prone to develop oral carcinomata too. Levin (1957) stressed the importance of differential diagnosis between, what he terms, "leucoplakia" and oral lichen planus, stating that the hyperkeratosis is a localised lesion confined to the oral cavity, whereas lichen planus is not always so.

(e) Syphilitic Mucous Patches of atrophic glossitis may resemble the atrophic form of lingual lichen planus. Biopsy may aid here, but serologic tests should be instituted if the slightest doubt exists.

(f) Moniliasis: The lesions of this disease can be scraped from the surface, whereas lichen planus lesions cannot. Moniliasis can be proved by the presence of numerous budding cells and filaments in a smear, and by positive culture of the material.

Despite the apparent facility with which differential diagnosis, from the above short descriptions, may be made, some cases may present great difficulty. Wade (1962) would not commit himself to naming one particular condition with which he was confronted; he, however, eliminated all other possible diseases except bullous lichen planus

and pemphigoid. Cooke (1960) had previously divided bullous lesions into intra-epithelial and sub-epithelial and a combined group. As the bullous lesions of lichen planus are sub-epithelial, the bullae of any disease requiring differentiation from lichen planus must be sub-epithelial, too. Of the possibilities, therefore, Wade eliminated epidermolysis bullosa and erythema multiforme clinically, biopsy having revealed no more than a picture of non-specific chronic inflammation. He was thus "left" with only pemphigoid and bullous lichen planus. Nikolsky's sign, usually indicative of pemphigus, was not present in this case. The appearance of white lines in the gingivae, together with a violaceous effect was suggestive of lichen planus. Wade did not mention the presence or absence of ocular lesions, but stated that skin lesions were not apparent. Oral lesions were chronic.

The author feels that the striae and violaceous hue could be indicative of lichen planus, but other manifestations could present later.

11. Therapy.

No cure is known for lichen planus. Some writers mentioned the use of compounds of arsenic, mercury and bismuth, saying how little success was achieved. Vitamins A, D and B complex have been used with indifferent results, although Ziskin and Silvers (1945) reported a good result with Vitamin A. and estrogens, the "desquamative gingivitis", sometimes accompanying lichen planus, being aided too.

Radiation therapy, which Orban and Wentz reported as having some value, has been used, superficial therapy at the rate of 75 r-units to each field at weekly intervals for six to eight weeks, being employed. Even antibiotics have been tried without helpful effect. At present the results of corticosteroid hormone treatment are indefinite but symptomatic relief follows in the bullous or erosive type (McCarthy and Shklar).

Kutscher and Zegarelli (1957) used local analgesic troches in the painful cases of erosive lichen planus. To help also in these cases, a relatively non-irritant topical anaesthetic - topical antibiotic is used to overcome possible secondary infection: bacitracin or polymixin B is recommended. Bland diet, avoidance of tobacco and alcohol and adequate sleep is urged. Pindborg (1959) said that the administration of arsenic and the intramuscular injections of magnesium thiosulphate produce cures, but this is not proven universally.

The disease seems to be psychosomatic in origin and if the emotional state of the patient is controlled, regression is often achieved. Tranquillisers could be of value, therefore, together with patient reassurance, as a high percentage of sufferers has cancerphobia. Warin, Crabb and Darling (1958) felt that, when discussing therapy, because of the probable psychosomatic cause, it is impossible to exclude the likely effects of "suggestion" when using drugs - the fact that a drug is being used, may cause an emotional patient to become calm and the disease thence to regress, the particular drug having no effect per se. Again, as the disease is basically chronic and has

periods of exacerbation and remission, some therapy used at a time of remission may be given unwarranted credit. Of 45 patients they examined with lichen planus of the oral cavity, the condition was completely cured in only four (4): in two (2) after 14 years, in one (1) after 2 years and one (1) after 6 months. Four (4) others had minimal lesions after 10, 5, 3 and 2 years respectively. Any cures seem to be spontaneous.

D. LICHEN SCLEROSUS ET ATROPHICUS.

General:

Miller (1957) said that the first description of lichen sclerosus et atrophicus was given in 1887 by Hallopeau.

There seems to be much doubt as to the occurrence of this disease in the oral cavity at all. McCarthy and Shklar (1964) stated that in most cases the microscopic features have not been typical of lichen sclerosus et atrophicus in oral conditions thought to be this disease, but have resembled, histopathologically, either lichen planus or even a keratosis. They mentioned an association between lichen sclerosus et atrophicus of the skin and lichen planus of the oral mucosa in the few cases reported and had doubts as to the actual occurrence of oral lesions of lichen sclerosus et atrophicus. However, Miller (1957) reported a case of bullous lichen sclerosus et atrophicus with vulval, anal, skin and oral manifestations. He emphasised the difference between early and older lesions as to their histopathological appearance which, in the case of the older lesions, was far more typical, featuring degeneration, rarefaction and destruction of elastic fibres. The

clinical appearance, too, as the lesions aged, was not like lichen planus - the lesions were well demarcated, greyish-white areas, one on the left buccal mucosa being 2 cm. in diameter. This area was entirely smooth and soft and composed of delicate, coalescent papules without surrounding reaction. The lesions in the mouth were asymptomatic. Miller believed this case to be the second ever described and the first with histopathological evidence.

The writer feels that if it is possible to confuse lichen sclerosus et atrophicus, lichen planus and a keratosis, biopsy of oral lesions should be routine.

This reviewer has found little mention of the disease in textbooks of Oral Pathology, except the small paragraph of McCarthy and Shklar (1964) and the following summary of a description of the condition by Orban and Wentz (1960), who felt it may occur as a definite oral manifestation and is a definite entity.

Clinical features:

This disease is a non-infectious, inflammatory condition appearing as small, white, flat papules, which may coalesce to form slightly raised plaques. The white surface becomes atrophic and wrinkled.

Course of the disease:

Lesions are mostly found on the vulva, penis or peri-anal areas. Havits and Welsh (1958) reported three cases occurring in the mouth, all on the buccal mucosa, two of which had lesions elsewhere on the body. One they believed to be the first report of lichen sclerosus et

atrophicus with only mouth lesions. The patient, a 24 years old white man, said that the lesions had been present in his mouth for four months. Examination showed white atrophic plaque formation on the upper right buccal mucosa, from the angle of the mouth to the anterior pillars of the fauces, with a few white atrophic areas on the palate.

Aetiology:

is not known.

Frequency:

The systemic disease is considered rare, but when found, usually occurs in older women.

Histopathology:

There is a sclerotic connective tissue zone below the epithelium, which zone is poor in cells, elastic fibres being absent. Lymphocytes and histiocytes infiltrate and surround the lesions. The epithelium is atrophic with complete absence of epithelial ridges, but with some hyperkeratosis.

The differential diagnosis would be:

1. Lichen planus
2. White patches of keratoses
3. Lupus erythematosus (chronic discoid)
4. Moniliasis.

SECTION 6.

INHERITED KERATOSES.

- A. WHITE SPONGE NAEVUS
- B. HEREDITARY BENIGN INTRAEPITHELIAL DYSKERATOSIS
- C. PACHYONYCHIA CONGENITA
- D. INHERITED KERATOTIC LESIONS (Unnamed).

INHERITED KERATOSES

A. WHITE SPONGE NAEVUS

1. Introduction:

It was Cannon who first called attention to this condition in 1935, calling it a "white sponge nevus of the oral mucosa".

It has since been called "congenital leukokeratosis of the oral mucosa"; "leukokeratosis oris"; "nevus sponosus albus mucosae"; "congenital keratosis of the gingiva" (Trott, 1956); "pachyderma oralis" (Kinney and Derifield, 1956); "familial white folded hypertrophy of mucous membrane" (Zegarelli and Kutscher, 1957); and "white folded gingivostomatosis" (Everett and Noyes, 1953; Orban and Wentz, 1960; Darling and Fletcher, 1958). The condition was described by Cooke (1956) as an "oral epithelial naevus". The term "familial white folded dysplasia of the mucous membrane" (Zegarelli et al, 1961), has also been used.

Lesions are classified as belonging to the group of congenital ectodermal dysplasias.

2. Clinical Features:

This condition of the oral mucous membrane is characterised clinically by a deeply folded or corrugated mucosa covered by a greyish-white, spongy keratotic-appearing surface. It is relatively uncommon and appears to follow an hereditary pattern as an autosomal dominant trait (Shafer et al, 1963). The lesions are almost always asymptomatic, except when desquamation and vesicle formation may occur and give rise to a burning pain.

Superficially, the lesions are often spread over almost the entire oral mucosa, or may be distributed in patches, in which latter

case the lesions may grow with age. The most obvious involvement is usually on the buccal mucosa, floor of the mouth and ventral surface of the tongue. The disease is often congenital, whereas it does not appear sometimes until infancy, childhood, or even adolescence, by which time it has reached full severity. Cooke and Morgan (1959) and Cooke (1956 B) found that it was commonly reported that a sufferer's mouth felt "rougher" in the morning than at other times, varying too, in texture throughout the day. They mentioned that the white "sodden" areas could be wiped off without causing haemorrhage. Cooke felt that these "naevi" were harmless.

Lesions have been reported in the same person in areas other than the mouth, such as the vagina, labia, anus and rectum (Everett and Noyes, 1953), (Zegarelli and Kutscher, 1957); even the nasal mucosa has been involved (Shafer et al). Yet, as Zegarelli and Kutscher (1957) pointed out, the names sometimes given to the condition suggest only oral involvement. It would seem that any "locality" identification, routinely used, pertaining to other than "mucous membrane", should be omitted.

All lesions thus far reported have remained benign in character and when maximum severity is reached, no further changes in the lesions occur during the person's lifetime (Zegarelli et al, 1961).

3. Histopathology

It has been stated that the histological findings are distinctive and diagnostic (Colby et al). Shafer, Hine and Levy felt the pattern is characteristic but not pathognomonic, McCarthy and Shklar (1964) that the picture is non-specific, and Stones (1962) stated that the

only typical feature is a lack of inflammation in the corium.

Darling and Fletcher (1958) biopsied an affected, but non-traumatized, area of the buccal mucosa and found swollen and distorted rete pegs with a well-marked, intact, lower rete border. The epithelium showed a considerable degree of parakeratosis, the superficial squamæ having a "shaggy" appearance due to fragmentation, thought to be the result of defective maturation. The dermal papillae showed a very mild degree of lymphocytic infiltration, but this was within normal limits and there was no sign of inflammatory change in the deeper sub-mucosa.

Cooke (1956 A) speaks of two main histologic characteristics:

1. An increased rate in the production of keratin, giving the keratin layer a "basket weave" pattern-
- or 2. There is a failure of the keratin to separate.

Cooke also stressed the normal appearance of the corium. In Cooke's second category, a peculiar dyskeratosis below the granular layer may be seen that would appear to impair the mechanical properties of the epithelial layer, so that it splits, exposing the underlying corium. Cooke and Morgan, in 1959, stated that it is becoming apparent that there are two or possibly more clinical entities grouped under the title "oral epithelial naevus", the first, histologically, being described as possessing a mucosa showing hyperkeratosis: the second, parakeratosis. These are the two categories outlined in 1956, when in two articles published in that year, Cooke described the first as being characterized by a wrinkled, white patch of the oral mucosa resembling undulations left on sand by the tide. No family history of the disorder

was discovered, only localised areas of mucosa being affected, usually symmetrically. These seemed to be simple developmental defects and could, in this author's opinion, be classified as either idiopathic hyperkeratosis or un-named or un-classified hereditary keratotic lesions.

The second group comprised cases similar clinically and histologically to cases reported by Everett and Noyes and Darling and Fletcher. Family history of the condition was shown and the whole of the oral mucosa could be affected, usually symmetrically.

Cooke, and Cooke and Morgan stated that though hydropic degeneration of the prickle cells of oral mucosa is not uncommon, it is a distinctive and constant finding in these cases.

Trott (1956) reported a case in which the biopsy revealed marked hyperkeratosis, the stratum corneum accounting for nearly half the total thickness. In the cells of the stratum granulosum, the nuclei showed pyknotic changes in some areas, the cytoplasm containing heavily staining kerato-hyaline granules. NO acanthosis was observed in the prickle cell layer and the basement membrane showed out well. He did find a slightly chronically inflamed corium, but the infiltration was well removed from the basal layer of the epithelium, from which he inferred, together with the lack of acanthotic change, that the hyperkeratosis was non-inflammatory in origin.

Most writers speak of the characteristic and marked spongiosis in the epithelium and parakeratosis, not hyperkeratosis, in the stratum corneum: however, they also agree to the lack of an inflammatory

infiltration in the corium.

Darling and Fletcher (1958) found spaces in the deep layers of the stratum spinosum, adjoining the stratum germinativum, either within the layer itself, or separating the prickle cell layer from the germinativum layer. The spaces were filled with a serous exudate and were somewhat reminiscent of the intra-epithelial vesicles found in herpes simplex and of the lacunae in Darier's Disease. However, no skin lesions existed or corps ronds demonstrated in the biopsy. These vesicles were seen at times to be joined to form quite large spaces, but at all times any vesicle was intra-epithelial. They found polymorphonuclear neutrophils in the submucosa, but related these to repeated irritations from defects in the epithelium. This vesiculation they explained as indicative of dyskeratosis, not virus infection, as hydropic degeneration is entirely compatible with dyskeratosis. Any changes in the membrana propria, consisting of hyalinisation of the fibre bundles in the reticular layer and any lymphocytic infiltration, are secondary and caused by long continued chronic irritation.

4. Aetiology

As previously stated, white sponge nevus is an inherited disease. However, Trott (1956) and Everett and Noyes (1953) have reported cases in which no family history of inheritance was present 1. among parents or children of the sufferers, in the case of two brothers, or 2. in the parents of a single girl. The disease may therefore have a recessive trait perhaps.

With increasing knowledge, says Witkop (1964A and 1964B), the pathogenesis of an increasing number of hereditary diseases is being

defined, so that rational, rather than empirical, therapeutic measures can be designed. Understanding of the consequences of altered genetic information implies possibilities for the control and investigation of genetic disease.

5. Incidence

Trott (1956) said that analysis of the few cases reported shows a higher incidence in females, but it is felt that as only about 23 cases are, as yet reported, (McCarthy and Shklar, 1964), it is rather premature to make any definite conclusion.

6. Differential Diagnosis

Certain early keratotic conditions in the mouths of tobacco users may somewhat resemble white folded dysplasia of the oral mucosa. Zegarelli, Everett and Kutscher (1961) drew particular attention to the so-called "tobacco pouch" lesion of tobacco chewers. They stated that the histologic findings in such a lesion suggest a hyperplastic response on the part of the epithelium, with some dyskeratosis. Possible disappearance or reduction of the "tobacco pouch" after discontinuation of the tobacco chewing habit makes clinical differentiation easier, as the histologic findings resemble "white sponge nevus" in some respects.

Darling and Fletcher (1958) felt that the differential diagnosis from lichen planus and the keratoses may be very difficult. Some cases of white sponge nevus have shown a fine lace-work pattern or even white streaks, but in the case of these latter, not the characteristic Wickham's striae of lichen planus. They felt that biopsy in doubtful

cases would establish a firm diagnosis, "as both lichen planus and 'leukoplakia' show typical inflammatory changes in the corium." This may be the case in lichen planus, but it is felt that it may not be so for the keratoses which need not show any histologic inflammation of the corium, a condition which they said applied to familial white folded gingivostomatosis, i.e. lack of inflammatory infiltrate. That the keratoses can be ruled out in differentiation on the basis of clinical appearance and age (McCarthy and Shklar) seems a very presumptuous statement (Author).

Thrush may be distinguished from the condition by smear examination, which reveals the organisms, either in spore or mycelial patterns. Histological examination for thrush would show destruction of the superficial epithelial layers, the presence of the fungus and the inflammatory response as an added aid. In addition, monilial plaque areas are easily scraped off the mucosa, leaving an ulcerated zone. Cooke and Morgan (1959), as mentioned earlier, found that the white lesions could sometimes be wiped off in white sponge naevus, too, but no ulceration or haemorrhage resulted. In cases of white sponge nevus, monilia can sometimes be demonstrated in patients who have been wearing a denture for some time.

7. Therapy

There is no treatment (All authors). Palliation is helpful, by eliminating any hot, spicy foods or smoking. Administration of Vitamin A was tried unsuccessfully.