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LEPROSY OF THE UPPER RESPIRATORY TRACT

DISCUSSION OF EARLY AND MODERATELY ADVANCED CASES¹

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Leprous processes may simulate the changes that take place in the mucous membrane affected by subacute and chronic processes of more common occurrence. Though it is believed that the incidence of leprosy is very low in continental United States, there is ample evidence that cases of it are passing through well conducted clinics under improper labels, and the facility with which transportation is carried on with countries of the Pacific, Mexico, Central America and South America foster the introduction of the disease in spite of the screen of ship quarantine inspection.

It has been my privilege and opportunity over a period of seventeen years to observe and study the conditions of the eye, ear, nose, throat and larynx of practically every patient certified as leprosy in whom the diagnosis was proved by painstaking investigation in the Receiving Hospital for leprosy patients at Honolulu, to which an average of from fifty to seventy new patients are admitted annually, and in which there have been between 125 and 200 in residence for periods of from one to eight years. I have also examined, studied and treated large groups of patients among from 450 to 600 in the Settlement at

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Molokai during these years, by periodic visits of from seven to fourteen days' duration on many occasions.

CLASSIFICATION

The traditional classification of leprosy has been made on the preponderance or presence of clinical evidence and is differentiated by three types, nodular, maculo-anesthetic and mixed. A more current grouping has been made on a similar basis and distinguishes cutaneous and neural cases. During the past two years much discussion has arisen over classifying cases in which there are lesions that have been named tuberculoid lesions or leprides. The clinical type of the case is of interest to the rhinologist and laryngologist because of the accompanying changes in the mucous membranes. However, similar manifestations may appear in cases of different types. The latter observation is in keeping with the view of the authorities who regard the disease as a general infection in which neural, cutaneous and tuberculoid lesions occur and represent only the phases or degrees of the same pathologic process.

PATHOLOGY

The essential histopathologic change of the disease is the involvement of the nerves, skin and mucous membranes by inflammatory processes which are characterized by perivascular infiltration with round cells and by a localized or diffuse "myxedematous" infiltration in which "foam cells," histiocytes and giant cells occur in varying frequency and number. Distributed through many of these infiltrations, in intercellular and intracellular locations, are single or clustered bacilli which are acid fast to stains. The aggregation of these infiltrations constitutes the granuloma of leprosy, or the leproma. Granulocytic leukocytes are found only infrequently in uncomplicated lepromas, and the central necrosis or colliquation which occurs in the granuloma of tuberculosis is rarely seen. The infiltrations appear primarily in the perineural and intraneural supporting tissues, in the deeper layers of the skin and in the tunica propria and submucosal layers of the mucous membranes. As they progress they invade the entire structures and distort or destroy them or, on the other hand, probably through interference with their innervation or nutrition, stimulate hyperplasia or cause them to atrophy. Thus follicles and glands of the skin and glands of the mucosa usually become atrophied, or even completely obliterated ultimately, but

may become hyperplastic during a stage of the process. Destruction of the elastic elements and the formation of scar tissue result in a flabbiness and a thinning of the membranes. Epithelium may become hyperplastic, thickened or keratinized, and its appearance suggests that produced by other chronic irritations. On the contrary, it may be thinned out to a single layer of cells which is easily brushed off and leaves a denuded surface. The extension of the process beyond the membranes is of particular interest in the nose and larynx because of the contiguity of the deeper layers of the membranes with the perichondrium of the septum, laryngeal cartilages and stroma of the vocal cords.

The gross pathologic appearance seen in the mucosae is that of thin, pale, dry membranes, diffusely thickened, reddened, soggy membranes or nodular thickenings of similar nature, both with and without ulceration. Invasion of the cartilages mentioned is followed by their atrophy or destruction, as observed in the frequent perforations of the nasal septum.

COURSE

It is characteristic of leprosy to present many acute phases and many spontaneous recessions. In the nose, the disease progresses by stages of activity and recession. A severe acute reaction with nasal blocking, edema and swelling may occur and last for several weeks and be followed by recession to an almost normal condition. During these apparently quiescent periods the nose may appear relatively normal, but close examination will reveal minor changes of the nature indicated on either the septum or the inferior turbinates. This acute attack may not recur for several weeks or months, but each time it occurs the structures become more and more infiltrated, nodular and ulcerated, and the normal tissues are replaced by the lepromatous mass or, as healing takes place, scars, distortions and narrowing of the passages develop. Similar processes occur in other mucous membranes.

Pain is not a constant symptom in leprosy but may be agonizing and persistent during the acute attacks of leprous fever (leprous reaction) for periods of several days or even weeks. The neuritic pain in the face, arms, hands, feet and back are much more severe than the pain of an acute "break-bone fever."

The onset of leprosy is apparently insidious in most cases but occasionally seems to be ushered in with an astonishing

suddenness. Its course, when once it is established, is seldom one of uninterrupted steady progression but rather that of advances and recessions. Probably in few cases are attacks of leprous fever or acute reactions of more or less severe degree escaped. It is to be remarked that even with the advanced and extensive manifestations there is little suffering from pain in other than the attacks of neuritis or arthritis. These may occur during the attacks of leprous fever as accompaniments of the cutaneous eruptions previously mentioned. When present, the pain along the course of the peripheral nerves in the arms, hands, legs and feet may be most severe and resistant to sedatives of such potency as morphine. These acute reactions with neuritis, giant urticaria, cutaneous edema, swollen, bluish red hemorrhagic mucous membranes, eyelids closed by edema, with photophobia and streaming tears are distressingly impressive to the medical attendant. However, they usually persist in such intensity for relatively short periods and are often succeeded by recessions of the lesions and prolonged periods of apparent quiescence, though they may be the initiation of steadily progressive changes.

It is also not unusual to see very advanced lesions of a more chronic type, which appear to be destined to a chronic and destructive course, subside in a few weeks to such a degree that even a fairly critical examination of the patient by one who is inexperienced may result in failure to detect the disease.

These fluctuations in the course and manifestations in the skin and nerves have parallels in the mucous membranes and structures of the nose and throat. However, though edema may subside, nodules recede and ulcers heal, there are scars, atrophies, distortions and mutilations remaining in proportion to the severity of the process and to the structure or function of the tissues affected.

CLINICAL OBSERVATIONS

Nasal.—Careful studies of the mucous membrane will reveal that practically every leprous patient has some nasal lesion due to leprosy. This opinion is concurred in by many observers, among them Del Rio (1), who showed that "the nose was affected in 82 per cent," although he does not state the type of case.

The symptoms that the patient presents are those of dryness, stuffiness, excessive crusting, blocking and epistaxis. All these conditions may be present in modified form in children, but

epistaxis and nasal crusting occur most often. The epistaxis may be the most significant complaint to bring the patient to the physician and is undoubtedly influenced by nose picking among children. As the child reaches adolescence, the symptoms are prone to increase markedly, since active leprosy is evidenced more during this period of life and in young adults. Among mature and older adults the symptoms may be those of the complications and sequelae of the more active processes.

The conditions observed within the nose tend to vary in accordance with the predominant clinical manifestations. Among the neural types the mucous membrane is swollen, pale, dry or relatively dry during active progressions, and it is not uncommon to note practical freedom from pain on manipulation of the nasal membranes. Ulceration is not common in the primary neural types, but it does occur in those nodular cases in which healing has occurred and which have become residual or secondary neural forms. Perforation of the septum is frequently found in this secondary neural type, with atrophy and crusting that closely resembles the ozena so familiar to all rhinologists. However, there is no assurance that the ozena of leprosy is of specific leprous origin.

Among the nodular types the mucous membranes are markedly reddened, or a bluish gray. They are usually moist but may be dry and present evidence of deep infiltration and nodulation. The membranes impress one as soggy and are covered with crusts, either with or without ulceration, and have a tendency to bleed with the slightest trauma. The principal sites of the nodules are the anterior third of the septum and the anterior half of the inferior turbinate. They are also found on the lateral walls. The middle turbinates seem to be involved less frequently.

The sinuses do not appear to be attacked by the disease, and I have not seen a case of sinus disease that seemed to be caused by a definite extension of a leprous process rather than indirectly by the results of the process within the nose or by other conditions. Though the long bones of the hands and feet are frequently included in the leprous processes, it is uncommon to find the changes in the flat bones such as those of the nose.

Murdock (2) made a survey at Kalihi Hospital of fifty cases in which there was marked involvement of the soft tissues of the nose but observed no instance of involvement of the nasal bone. With the cartilaginous septum, however, it is quite differ-

ent, since large perforations occur in it and extend as far forward as the tip. I have seen several cases in which the entire cartilage had been perforated and destroyed and the nasal tip had become a loose, flabby and formless mass of tissue (Figs. 1 and 2).

As healing proceeds, much scarring occurs and may be accompanied by great distortion. The intranasal structures may become adherent by dense synechiae and crusting, and the nasal passages may be completely obliterated. Partial or complete collapse of the alae may result from paralysis of the elevators of the wings and angle of the mouth in lesions of the seventh nerve.

Acute leprous reactions with marked edema of the nasal mucosa, sudden epistaxis and edema of the face, ears, neck and extremities may occur. These acute reactions are accompanied by high fever, chills, agonizing neuritis and arthritic pains, and efflorescence of cutaneous lesions, varying from those of morbiliform character, erythema nodosum or acute cellulitis, and may be complicated by acute swollen nerve trunks and evidence of acute arthritis.

Pharyngeal.—There is a remarkable freedom of symptoms with leprous involvement of the pharynx unless the patient is suffering with an attack of "acute leprous reaction." More rarely the palatal muscles may become progressively paralyzed during the very late stages of the disease and cause the characteristic regurgitation of fluids through the nose and the nasal voice.

Definite changes in the mucous membrane are rarely observed among the neural types. During the acute attacks of leprous reaction the palatal muscles may become paretic or paralyzed, and with the subsidence of the attack there may be an astonishing return of function. Nodular types frequently present changes in the mucous membranes of the pharynx. Nodules commonly occur in the earlier stages at the base of the uvula (Fig. 3), extend into the folds above the tonsils and subsequently spread over all parts of the soft palate (Fig. 4). In later stages they spread forward over the hard palate (Fig. 5) and form broad ridges of nodular infiltration along its center even to the alveolar areas (Fig. 6). The teeth become loosened and are partially buried by the nodules. On the other hand, the lingual surface of the alveolar processes of the upper central incisors is frequently involved early in this process, and the extension of the infiltration is backward along the ridge of the palate.

The nasopharynx shares in the process by extension, and nodules may be seen high on the posterior nasopharyngeal wall in those cases in which the thickened soft palate does not interfere with examination by the mirror.

Lingual.—Few symptoms are complained of in leprosy lesions of the tongue. Neural involvements of the tongue are not seen, but nodules are (Fig. 7), usually in the anterior third and late in the disease. Leukoplakia is also quite common in the same location and occurs late. These areas of leukoplakia are often quite anesthetic to tactile stimulus. Ulceration occurs when nodules have broken down, though they are usually quite superficial. Rao (4) describes "macroglossia" in which, instead of definite nodules, the whole tongue may be enlarged owing to a generalized infiltration of the whole organ, which he feels corresponds to the "leontiasis" type of cutaneous lesion affecting the whole face. I have not seen this type of lesion, but I have seen thickened and deeply furrowed tongues (Fig. 8), which may be analogous.

Del Rio (1) states that "the tongue was affected in 20 per cent, nodules being observed in 15 per cent and cicatrices in 5 per cent," but my patients have not shown so high an incidence of these lesions.

Tonsillar.—As a result of our studies (3) and subsequent observations we have concluded that more than 20 per cent of leprosy patients have demonstrable infiltrative and nodular lesions of the tonsils (Fig. 9) which are of leprosy origin because of specifically proved associated changes.

Laryngeal.—Approximately 40 per cent (3) (substantiated by subsequent observations) of the moderately advanced nodular cases present leprosy lesions of some form in the larynx, and in the vast majority of instances the epiglottis is involved. A great majority of the more advanced cases present laryngeal lesions. The characteristic early symptom is "the leprosy huskiness," a peculiar vocal quality that strikes the experienced as suggestive. The patients complain of a dryness and a tickling sensation that causes a dry, unproductive cough.

The mucous membrane of the neural type is dry and a grayish red, and the surface is often covered with a frosty exudate which is thin enough to allow the red membrane beneath to shine through. It does not become ulcerated as in the nodular type, but it may become atrophied to some extent. The latter observation has apparently been noted also by Sechi and Giunti,

(5) who state that "in neurotic leprosy, however, one will find only the usual atrophic alterations." In the early nodular type the epiglottis is attacked early on both its anterior and posterior surfaces (Fig. 10) and extension occurs into the surrounding parts by contiguity along the aryepiglottic folds, the arytenoids and posterior commissure. In early cases the anterior parts appear to be affected first, but in the later stages one may see a dull, gray, nodular tissue within the entire larynx. The arytenoids stand out in the process later by becoming almost immobile, large and hard with infiltrations (Fig. 11). Single large nodules form characteristically along the lateral border of the epiglottis. The cords become swollen when nodules involve the lateral bands, as often happens, and the nodules commonly invade the ventricles and vallecula. Nodules in the cords are probably more common than is known, but they are seen rarely because they occur late, when the distortions and infiltrations of the structures above obscure their observation.

The recurrent laryngeal nerve escapes in most cases (except during an acute reaction), while the superior laryngeal nerve is involved more often by deep infiltration in its branches of distribution. I have never seen a case of recurrent paralysis of the nerves which I was sure was due to leprosy. The motor nerves innervating the muscles of the upper part of the respiratory tract are seldom affected in other than very late cases.

Congestion, swelling, infiltration, nodulation, ulceration, atrophy and scar formation with contractures and distortions are the successive steps in the disease in the larynx as in all the other diseased parts of the mucous membrane.

Not infrequently in leprosy patients a severe edema of the larynx develops resembling that of some "allergic" phenomena in intensity and degree. Laryngeal stridor and edema of the glottis may occasionally result in fatal consequences. This acute reaction is also accompanied by high fever, chills, severe pain in the limbs and acute cutaneous lesions of many forms.

DIAGNOSIS

Though the diagnosis of leprosy can be made in many instances by clinical examination, it can be confirmed in most cases by bacteriologic examination. This can be made easily and quickly by the rhinologist with microscopic preparations.

The technic of making a nasal "snipping," which follows is comparatively simple: Use a semisharp Freer submucous ele-

vator under good illumination, press firmly enough to blanch the tissues under the blade and scrape hard enough to get some of the epithelium, since the bacteria are in the tissues; hence swabs collecting mucus are valueless unless ulceration is present. Spread the collected scrapings on a slide and stain by the Ziehl-Neelsen method of staining for tubercle bacilli. The favorite site for scraping is the septum, near the anterior border, or on the side of the nose immediately above the anterior end of the inferior turbinate. Blood in the specimen makes a poor microscopic preparation, and the attendant trauma may leave an intractable ulcer; hence bleeding should not be provoked.

Murdock (2) examined 164 patients by the foregoing method and 143, or 87.2 per cent, gave positive bacteriologic results, which is a higher percentage than would give positive results with cutaneous snips.

The same technic may be carried out when practicable in the examination of the pharyngeal lesions. When a well defined nodule exists in the soft parts, any form of ring punch may be used to remove the entire nodule for biopsy. This procedure may excite an intractable ulceration which might not otherwise occur; hence excision of a nodule of the mucous membrane should be resorted to only in unusual cases.

As a rule I depend on swabs for collecting bacteriologic specimens from the larynx. I have used the punch on nodules of the epiglottis, but here again there is the danger of starting up an ulcerative process.

In the event that these examinations of the nose and throat are undesirable, because of any of several reasons, contributory evidence of the presence of the disease may be obtained by "snipping" the skin of the lobe of the ear, even though no definite changes are detected in it. Snippings from the ear are easily carried out and yield reliable results if properly executed. I have found the best technic to be as follows: Grasp the lobe of the ear or the nodular area firmly between the thumb and finger of the left hand to blanch the tissue; have an "Ever-ready" reinforced back safety razor blade with a single cutting surface in the right hand; with the toe or point of the cutting edge, make a small nick into the area about 3 mm. deep, and while the blade is still buried in the tissues twist it out at right angles to the line of incision, carrying with it some serum and tissue cells wherein the bacteria are located.

In the event of failure to confirm the diagnosis in suspected cases by examination of the local lesions and the ear, one should make an inspection of the entire body, looking for associated lesions and making microscopic examinations of those cutaneous lesions observed. The skin of the brow and of the buttocks is affected very frequently, and the lesions found in these areas are often more advanced than those in other locations.

DIFFERENTIAL DIAGNOSIS

Leprosy is commonly mistaken for syphilis and until later years it was common experience to find that leprosy patients had had much antisyphilitic treatment before a diagnosis was finally made. This mistake was made because such a great number of leprosy patients gave a positive Wassermann reaction. More than 40 per cent of leprosy patients show a positive Wassermann reaction in the nodular types, without a history or other evidence of syphilis. I have observed negative Wassermann reactions on admission of leprosy patients to the hospital and have also observed that as the leprosy disease progresses the Wassermann, Kahn and other precipitation tests become positive and that the intensity of the test diminishes as the leprosy recedes. In the U. S. Public Health Service conference in which serums were submitted to Kolmer, Kahn, Eagle and originators of other tests, the results were as described.

Wayson, (6) who studied the subject at Kalihi Hospital, thinks that "most cases of advanced nodular or myxedematous types will yield positive serology." No evidence has been submitted to prove that patients with the neural type (except those secondary to the healed nodule) give more positive tests than other members of the general population of the same age, race and manner of living.

The therapeutic test may be resorted to in doubtful cases, but even this is not proof of syphilis. In the administration of arsenicals the leprosy condition may recede as in syphilis, though much more slowly. However, leprosy frequently recedes spontaneously without therapy of any sort and likewise after administration of intravenous treatment with nonsyphilitic agents.

A detailed word picture of the appearance of leprosy changes in the mucous membranes is difficult and one unconsciously forms conclusions from clinical "hunches" and experience with numbers of cases of the two other diseases whose underlying pathologic condition is classified as a granuloma, namely syphilis

and tuberculosis. I have had limited experience with laryngeal syphilis but have been fortunate through my association as attending laryngologist to an active hospital of 450 beds for tuberculous patients to be able to make comparisons between the tuberculous and the leprous process. Then too, many leprous patients have tuberculosis. In fact it is a common coincident infection and the two diseases are frequently present at the same time.

Leprous, tuberculous and syphilitic lesions of the larynx may resemble one another at one stage of their development. Tuberculosis almost always involves the posterior part of the larynx first, and the most frequent site is the posterior commissure. The arytenoids, folds and epiglottis are involved later. Leprosy involves the epiglottis first and the cords and arytenoids later. The anterior and the posterior surface of the epiglottis are affected alike. Tuberculosis is almost always very painful while leprosy is characteristically almost painless. In the earlier stages the mucous membrane is more hyperemic in tuberculosis and syphilis, while in leprosy it is pale and gray. Tuberculosis is bilateral as a rule; syphilis is usually unilateral and almost always involves the anterior structures, while leprosy may be either and when seen late is widespread, involving several parts. Syphilis quickly ulcerates, the ulcer being sharply defined with clearcut edges, the surrounding areas being smooth and highly congested. The larynx wherever involved with leprosy is definitely nodular, though ulceration may occur. When ulceration occurs, aided by secondary infection, the epiglottis may be destroyed (Fig. 11). However, one does not see the great destruction of tissue in laryngeal leprosy that one sees in tuberculosis or syphilis, with the same amount of nodular involvement. Leprosy tends to heal, and scars cause distortions in one area while the adjoining area is actively infiltrated with nodules. A leprous larynx may be intensely nodular and infiltrated and not break down, while in tuberculosis and syphilis no such extensive nodular infiltration takes place without early deep ulceration and breaking down.

While a differential diagnosis can be made in most cases, there are times when all local signs fail and one must depend on examinations elsewhere in nerves, skin and chest and in serology and bacteriology.

Care must be observed in making the bacteriologic diagnosis and it is sometimes necessary to resort to bacteriologic

cultural methods, since staining and morphologic characteristics are not sufficiently exact to differentiate the bacillus of leprosy from that of tuberculosis. Even animal inoculation may be misleading since the development of large lymph nodes containing acid-fast organisms may occur after inoculation with either of these bacteria. *Bacillus tuberculosis* grows readily and characteristically on suitable mediums. The bacillus of leprosy has probably never been grown on artificial mediums.

The presence of nasal deformities present striking differential points. I speak of the so-called saddle nose. If the bony septum is destroyed and absorption of the nasal bones occurs in syphilis, one may expect to find a sinking in or depression of the nose. In leprosy the bony septum is not destroyed; only the cartilaginous portion is involved, and in this type the nose sinks nearer the tip (Fig. 12).

It has been reported that the hard palate may perforate, but I have never seen a case which I considered was due to leprosy; syphilis yes, tuberculosis perhaps, but leprosy no.

TREATMENT

After having tried many of the remedies, including the heralded chaulmoogra oil, I have concluded that none of them act as a specific in local or topical treatment. Hygienic care of the mucous membranes, which resolves itself largely into methods of cleansing, and the accomplishment of drainage in the nose appear to assist uncomplicated healing and certainly give comfort to the patient. This general conclusion was reached after controlled experimental treatment which I carried out several years ago (3) on another large group of patients and has seemed to be substantiated by subsequent observations.

I have found that the patient who rests his larynx has less cough and irritation than one who indulges in talking and other vocalizing which amount to abuses of his larynx. I have used the spray of chaulmoogra oil directly into the larynx without favorable results. The use of bland oils by inhalation of the fine spray seems agreeable to the patient. Finally, the treatment of leprosy of the upper part of the respiratory tract is much the same as that of treating the same parts in a tuberculous patient, and, since the condition of the nose, throat and larynx reflects to a great extent the general condition of the patient, the treatment should in the main be directed toward improving the general condition.

The extent and degree of the studies and observations in leprosy on which this discussion is based were made possible through the cooperation and assistance of the officers of the United States Public Health Service, who have served as the medical staff at Kalihi Hospital, Honolulu, and the adjoining United States Leprosy Investigation Station. Much of my study has resulted from the stimulating influence, council and advice of Dr. N. E. Wayson, formerly director of leprosy investigation at Kalihi Hospital.

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DESCRIPTION OF PLATES

PLATE 11

[Numbers are as revised after eliminating two of the original illustrations, the original numbers being indicated in parentheses.]

FIG. 1. Total destruction of septum with sinking in of the nasal tip.

FIG. 2. Total destruction of the cartilaginous septum with similar mass of granulation tissue replacing the nose.

FIG. 3. Nodular infiltration of uvula with extension into the right supratonsillar fossa.

FIG. 4 (ex 5). Showing the progress forward of the infiltration of the soft palate.

FIG. 5 (ex 6). Much infiltration and distortion of the entire hard palate.

FIG. 6 (ex 7). The alveolar processes of the upper central incisors showing extensive involvement.

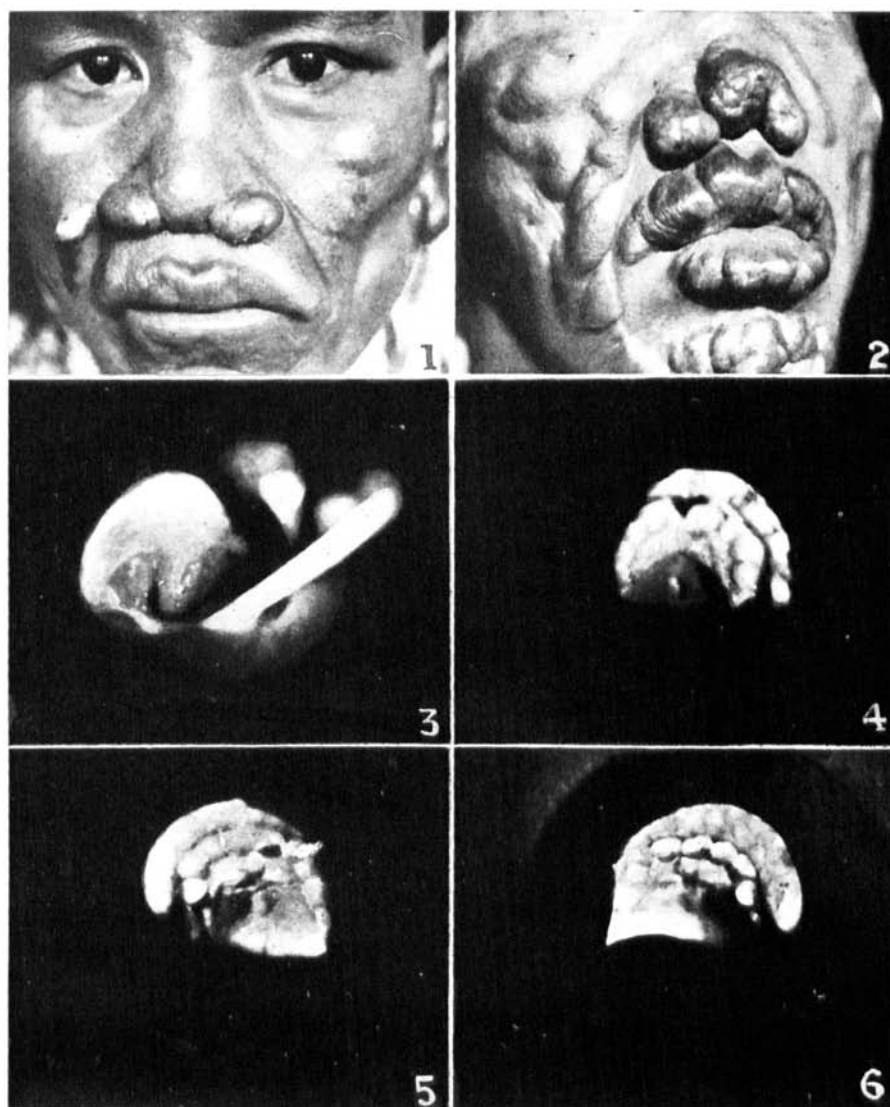


PLATE 11

PLATE 12

FIG. 7 (ex 8). Large nodular formation of the right half of the anterior tip of the tongue.

FIG. 8 (ex 9). Broad ridges with deep furrows and islands of leukoplakia involving the entire tongue.

FIG. 9 (ex 10). Extensive nodular infiltration of the right tonsil.

FIG. 10 (ex 11). The epiglottis infiltrated with nodules throughout its entire anterior and posterior surface and the arytenoids extremely enlarged and infiltrated with hard nodules.

FIG. 11 (ex 12). Advanced nodular infiltration with destruction of the central portion of the epiglottis.

FIG. 12 (ex 14). Leprous deformity of the nose characterized by destruction of the septal cartilage and sinking in of the nasal tip.

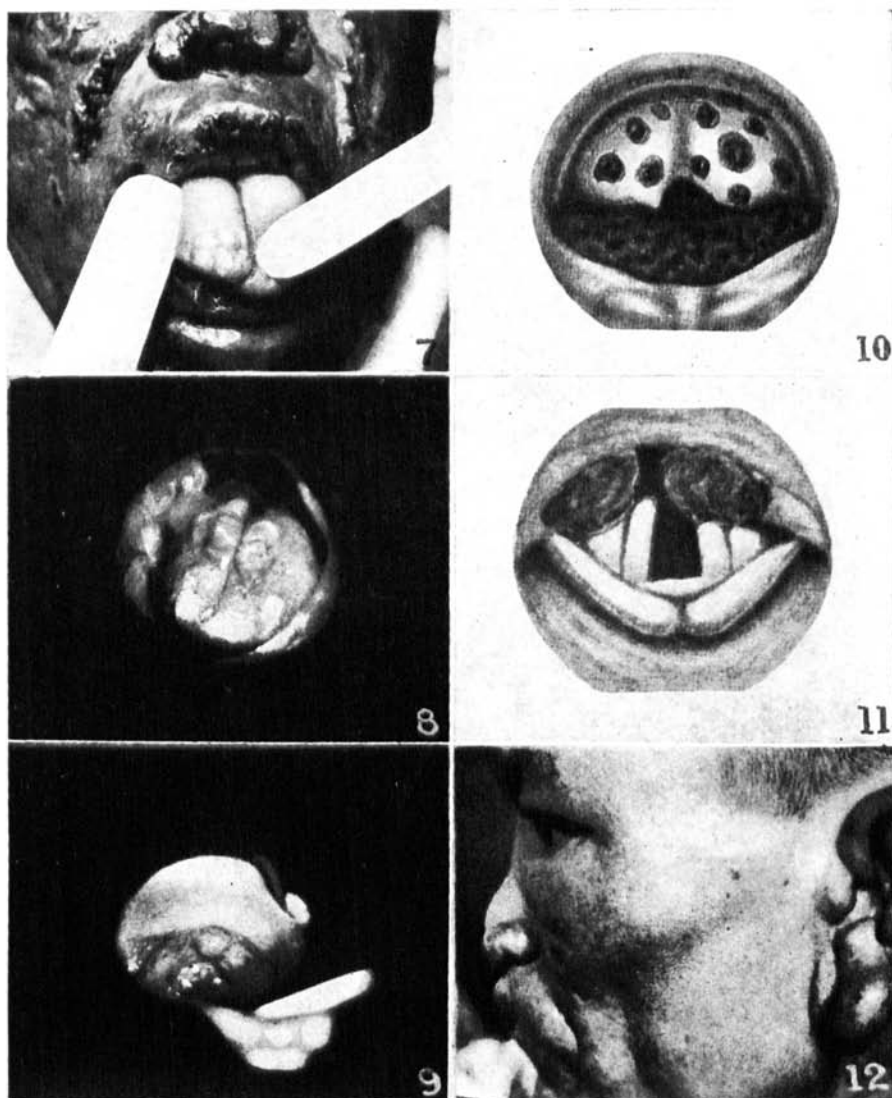


PLATE 12