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SYMMETRICAL LYMPHOMATA OF THE LACRIMAL AND SALIVARY GLANDS (MIKULICZ'S DISEASE.)*

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It is now twenty years since Mikulicz first described, in 1888, a characteristic and symmetrical enlargement of the lacrimal and salivary glands, chronic in character, of a noninflammatory and nonpainful type, and not associated with any demonstrable systemic disease. Four years later (1892) he contributed to the *Billroth Festschrift* a special study based on three cases of this rare disease, including the case reported by him in 1888, another reported by Haltenhoff in 1889, and a third which Fuchs had placed on record in 1891, to which he added a brief review of ten similar cases, and thus fixed in ophthalmic literature the characteristics of a disease which has since borne his name. The most important contributions since that time have come through the clinic of Mikulicz, Tietze in 1896 having reported one case, and Kümmel in 1897 having collected six additional cases which he presented in a review of the literature of the subject, comprising a tabulated analysis of twenty-one cases, including his own. Many interesting monographs have since been presented, including those of Axenfeld, Zirm, Bock, Pick, Hirsch, Fleischer, Baas, and others. Among these, that of von Brunn (1905) is probably the most complete, while Meller (1906) and Snegireff (1906) have each added some very interesting observations. Valuable contributions have also been made by certain French observers, the most important being those of Abadie, Delens, Gayet, Haltenhoff, de Lapersonne, Panas, Debierre, DeWecker and Masselon. A series of similar cases were briefly reported before the Ophthalmological Society of the United Kingdom (1887-94) by Power, Frost,

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Juler, Brailey, Silcock, Snell, Sandford, and Griffith; while in America interesting examples of this rare disease have been placed on record by Randolph (1897 and 1909), Osler (1898), Stieren (1901), Posey (1902), Shoemaker (1904), Cutler before this Society (1904), and Ziegler (1906).

SYMPTOMATOLOGY.—The disease is sufficiently described by its name—symmetrical lymphomata of the lacrimal and salivary glands. Mikulicz originally segregated cases in which the lacrimal, parotid, and submaxillary glands were symmetrically and simultaneously enlarged (Fig. 1). Later reports from his clinic, however, included cases that

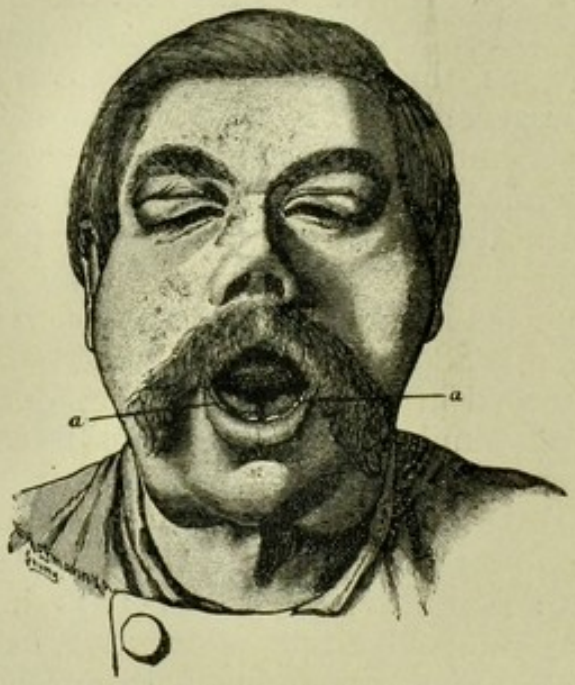

FIG. 1.—Symmetrical enlargement of the lacrimal, parotid, and submaxillary glands. (Original case of Mikulicz.)

were nonsymmetrical, and cases in which only a single pair of glands were involved. It is quite possible that these atypical cases might have developed lymphomata of the unaffected glands if they had been kept under observation long enough, without instituting treatment. This would seem to limit the characteristics of this symptom complex, therefore, to a chronic, indolent, symmetrical enlargement of one or more glands of the head, of a noninflammatory and nonpainful type, not associated with any systemic disease, beginning, as a rule, in the lacrimal, and soon involving the parotid and submaxillary glands. This sequence, however, may be reversed. The accessory lacrimal glands and the accessory parotids are frequently involved, while the

preauricular glands may participate in this process. The sublingual glands (Fig. 1, *aa*) and the glands of the palate (Fig. 2) have also been affected in many cases. Involvement of the Blandin-Nuhn glands may cause a distinct nodular swelling on the tip of the tongue.

Occasionally some of the other glands have shown enlargement, but their interrelation has not been proved. Osler noted enlargement of the spleen, of the cervical chain, and of the tonsils in his case. Sandford reported hypertrophy of the tonsils and adenoid tissue of the pharynx. Haltenhoff found marked tonsillar enlargement. I have likewise noted enlarged tonsils in both of my cases. Such conditions were usually antecedent, however, and neither synchronous nor associated. Otherwise, no evi-

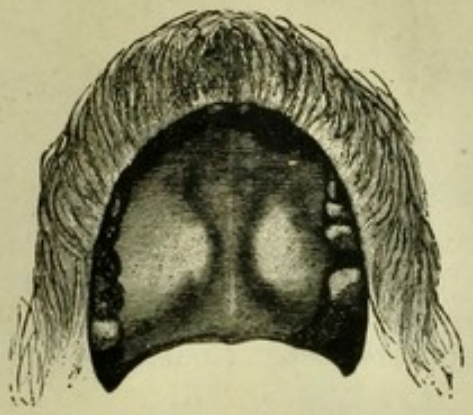

FIG. 2.—Enlarged glands of the palate. (Mikulicz.)

dence of a general lymphatic disturbance has been educed.

The objective symptoms of this disease are chiefly a dense, brawny swelling of the glands involved, nonpainful but sometimes tender to pressure, freely movable under the skin, but occasionally adherent to the subjacent tissues. The facial appearance is quite characteristic. There is a marked broadening of the cheeks as in mumps, and partial ptosis on the temporal side, the drooping eyelids resembling those of a bloodhound. Elevation of the lid at the external canthus often reveals a downward displacement of the retrotarsal fold by the swollen and pendulous lacrimal gland (Fig. 3). Both parotid regions are occupied by a broad, oval tumor, which may be knobby or lobulated, and frequently displaces the ear lobe upward and outward. The submaxillaries do not, as a rule, protrude on the skin

surface, but may become unduly prominent on the floor of the mouth.

The subjective symptoms noted in these cases are dryness of the conjunctiva from partial suppression of the tears, obstruction of the vision from ptosis, with consequent inability to see through the chink-like palpebral fissure, dryness of the mouth from lessened salivary secretions, and limited ability to swallow or talk owing to the interference of the enlarged submaxillaries.

Respiratory disturbances are not uncommon. Kümmel has noted hypertrophic rhinitis, bronchitis, asthma, and the sequelæ of influenza in several of his cases. Haltenhoff records eczema of the nostril, sneezing, coughing, swelling of the pharynx,

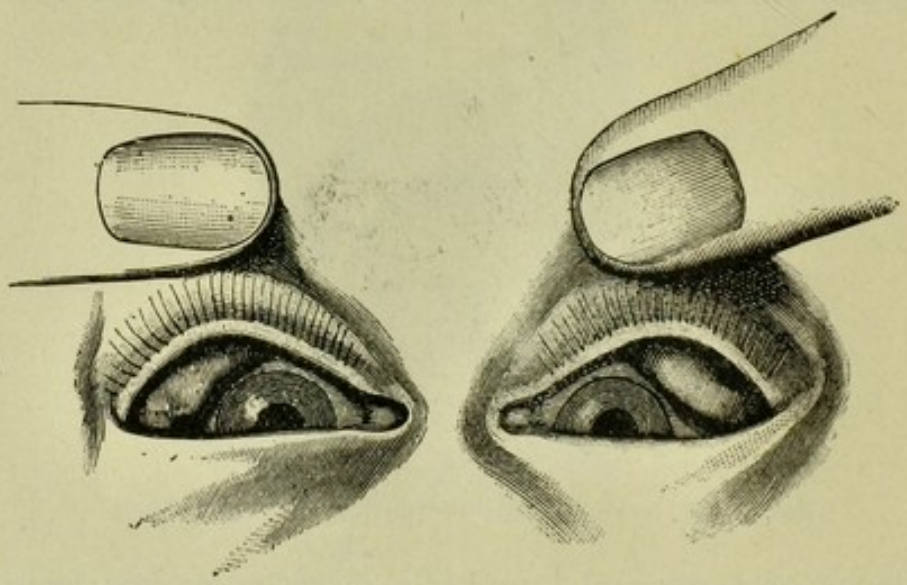

FIG. 3.—Downward displacement of pendulous lacrimal glands. (Mikulicz.)

and enlarged tonsils in his case. Adler relates that his patient suffered from hoarseness and swelling of the pharynx of so marked a character that a laryngeal examination could not be made. Osler mentions a nasal discharge, thickening of the cartilaginous septum, enlarged tonsils, and other obstructions to free breathing in the case he reports. Pick refers to a chronic cough with expectoration. Ranzi records a persistent postnasal catarrh. My first patient showed hypertrophy of the turbinates, antral discharge ,and intranasal adhesions, with unusually large tonsils. My second patient, herein reported, has a similar history of respiratory obstruction. Both were confirmed mouth breathers. Dryness of the lips and mouth has frequently been noted in these

cases, and may arise either from oral breathing or from lessened activity of the salivary glands due to pressure on the acini from interstitial deposits in the gland. Carious destruction of the teeth has been noted by Kümmel, probably caused by mouth breathing.

A summary of the cases reported shows that the age at which this disease was first manifested ranged from four years to seventy years. Males and females appeared to be affected about equally. The duration of the attack varied from two months to ten years and upward, which fact of itself would emphasize the chronic, indolent character of this disease. No constitutional disease has been found complicating these cases, when typical.

Report of Cases.—As I shall later refer to certain facts observed in my first case, I will include a condensed history of it.

Case I.—Agnes M., colored, aged eighteen years. Came to Wills Eye Hospital, January 13, 1905, with symmetrical swellings of the lacrimal, parotid, and submaxillary glands; duration six weeks. Palpation showed that glands were hard, not tender, and nonadherent. Slight ptosis. Lips dry. Tonsils very large but soft and relaxed, filling the postpharyngeal space and interfering with respiration. Was a mouth breather and showed facial pallor in spite of her color. Hypertrophy of inferior turbinates, with adhesions to septum and discharge from antrum. No systemic disease. Spleen not enlarged. Blood and urine normal. Visual acuity unimpared.

Treatment.—No medicine was administered, but tonsillectomy was strongly urged.

Operation.—On January 16, 1905, the tonsils were thoroughly excised. Free breathing was at once established. Retrogression of the submaxillaries began promptly, followed by the parotids, and finally included the lacrimals. Convalescence covered a period of about two months. Coincidently, she was wholly freed from her chronic head colds.

Case II.—David H., colored, aged thirty-four years, came to my clinic at Wills Eye Hospital, April 10, 1908, with bilateral enlargement of the lacrimal, parotid, and submaxillary glands, which began about eighteen months ago, and involved the glands in the order named. The swellings were symmetrical (Fig. 4), of a dense, boardlike hardness, nonpainful but tender on pressure; not adherent to the skin but attached to the subjacent tissues. There was some slight ptosis of the upper lids at the outer side, the drooping resembling that of a bloodhound. There were three small lymph nodes on the chest. Spleen was not enlarged. Sublinguals and Blandin-Nuhn glands were not involved.

There was puffing of the turbinates in both nostrils; tonsils were enlarged and soft; uvula was relaxed and pendulous; patient was subject to frequent head colds and was

a mouth breather. Extra exertion caused shortness of breath. Suffered from dryness of lips and mouth. For first six months, following onset of disease he had a bad cold with attacks of choking, also alternating attacks of diarrhœa and constipation. General health good. Blood and urine normal. Family history negative. Had never had any fevers or other serious illness. Had mumps in childhood. Occasional attacks of chilliness; no malarial history. Had not had syphilis. Injection of Koch's "old

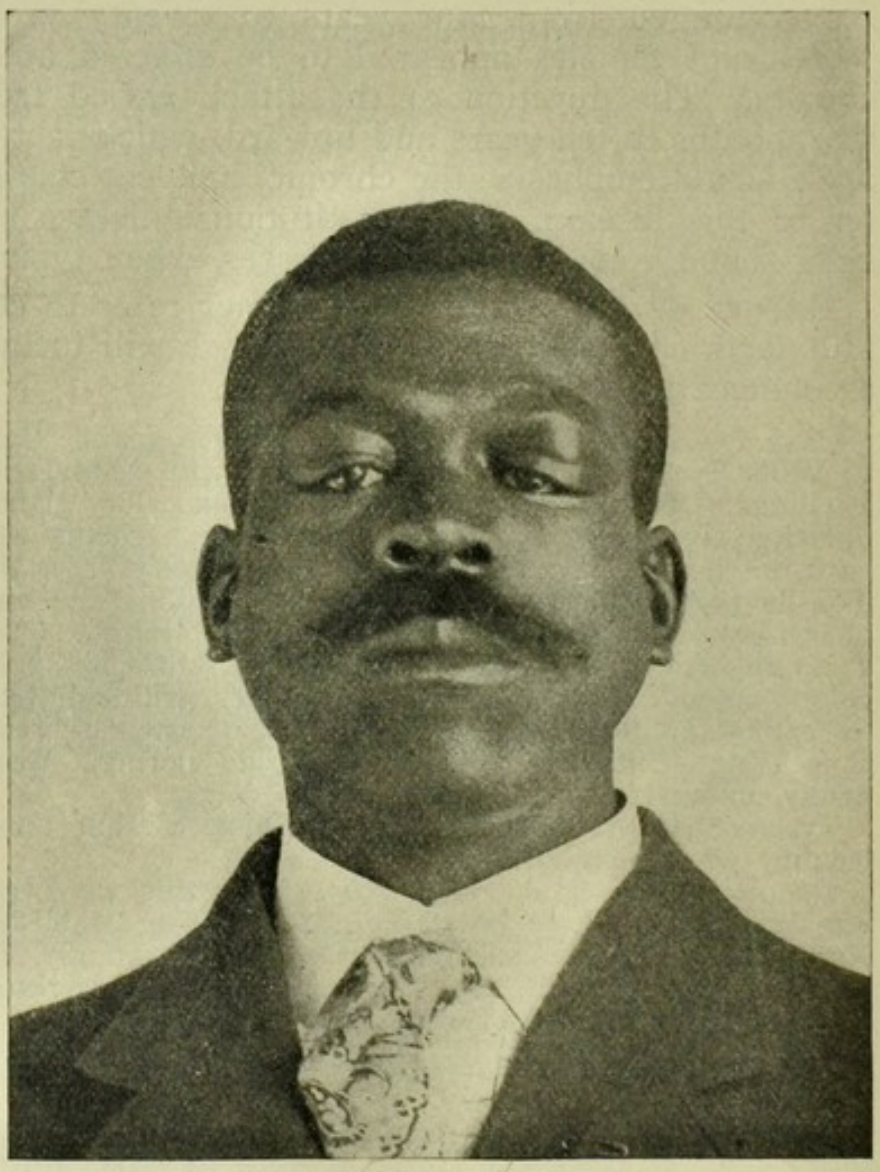

FIG. 4.—(Case II) Author's case of Mikulicz's disease.

tuberculin" gave negative reaction. By a control test the same tuberculin gave a positive reaction in two other cases on the same day, which demonstrated the activity of the test fluid and his freedom from tuberculous infection. Vision was practically normal.

Treatment.—I decided to withhold all medication, as in my previous case, and to simply restore nature's functions by resorting to operative measures.

Operation.—On April 15, 1908, double tonsillectomy was performed, and the uvula was excised. The throat healed rapidly, and the intranasal condition showed marked im-

provement. Free nasal breathing was reestablished and the physical condition improved. The first retrogressive symptom noted was the softening of the lacrimal and submaxillary glands, which began to be apparent about the time he was discharged from the hospital, May 11, 1908. The parotids still maintained their fibrous hardness, although the swelling was somewhat reduced.

ÆTIOLOGY.—The ætiological factors which most writers have recorded in these cases are: 1. Infection from buccal or conjunctival bacteria; 2, glandular irritation from some toxic agent in the blood or lymph stream causing lymphatic hyperplasia; and 3, some idiopathic origin. Mikulicz and Kümmel favor the theory of "an infectious or parasitical process in the widest sense of the word," but do not explain the origin of their belief. No specific bacteria have been demonstrated in these cases, the microscope usually revealing lymph cell infiltration of the interstitial tissue, which Mikulicz considers wholly responsible for the enlargement of the gland.

Although bacterial infection is usually accompanied by an acute inflammatory process, no inflammation has been noted in these cases. Granting the possibility of infection, whence would it originate—from the eye, the mouth, or the nose? It has been stated that trachoma of the fornix has caused lacrimal adenitis (Baquis). By analogy it is deduced that buccal bacteria might be transmitted through Steno's duct and thus infect the parotid (Hanau). I think it is much more probable, however, that the source of infection is nasal, and the means of transmission through the lymphatic capillaries. It certainly seems possible that a steady stream of toxic, bacteria laden secretions could be absorbed from the accessory sinuses (chiefly antrum) and carried directly to these contiguous glands. If, however, the origin is an infection from neighboring parts, why should the course of this disease be so sluggish and the condition remain unchanged for months and even years? On the other hand, may this not be a chronic hyperleucocytosis strictly localized to these enlarged lymph glands?

How can we explain the retrogression of these glandular swellings during the course of an acute intercurrent disease, and their recrudescence in some cases soon after convalescence? Kümmel has reported such an occurrence during pneumonia, Mikulicz during appendicitis, Haeckel through a severe enteritis, Delens after an attack of cholera,

Zirm during an attack of erysipelas which followed partial excision of the gland, Quincke from a similar cause, and Osler after an attack of acute pleurisy with effusion. I have seen slowly healing operative cases improve during an attack of facial erysipelas, and relapse to their previous condition when the attack was ended. This is particularly noticeable in operations about the nose, as the sinus discharges wholly cease for a time, but gradually reappear when convalescence is thoroughly established. The query naturally arises, does the general disease create a systemic polymorphonuclear leucocytosis that temporarily overwhelms and obliterates the localized hyperleucocytosis in the affected glands?

As to the question of hæmatogenous infection, Kümmel says: "There is in no case any reliable evidence as to the transmission of bacterial infection from the blood to the salivary and lacrimal glands." Other skilled observers who have made a careful study of the blood in these cases have likewise noted the absence of bacteria or other abnormal conditions, and thus corroborate this view. The fact that only the glands of the head are attacked would also militate against the probability of a bacteræmic origin, although it is not possible to explain the process of "pathological selection."

On the other hand, Mikulicz suggests the theory that the "disease exciter" is ectogenous, the port of entry being through the conjunctiva; hence the lacrimal gland is attacked first. From thence it passes by the lacrimal canal to the nose, nasopharynx, and mouth, which through their similar mucous membrane linings form a "continuum" that carries this agent to the other glands. In view of the fact that no specific infectious germ has been isolated, this theory of transmission seems too hypothetical to merit our acceptance.

There still remains for our consideration the view that some toxic agent or chemical irritant in the lymph stream might cause an occlusion of the efferent lymph channel of the gland, and thus encourage leucocytic engorgement. This could occur in one of two ways: 1, From some perversion of glandular function resulting in the secretion of irritating materials and their retention within the gland substance, and, 2, from irritation of the gland by some toxic fluid which is absorbed and transmitted from neighboring parts. Both of these processes

may be properly included under the general term of chemotaxis or toxic leucocytosis.

The first proposition has a typical exemplification in the case McHardy has placed on record, in which sudden enlargement of the lacrimal glands resulted from excessive indulgence in grief. Lagrange has reported a case of temporary enlargement of these glands due to the perverted metabolism of the menstrual period. We also know that the antrum may secrete a fluid so irritating that it will cause swelling of the Schneiderian membrane and excoriation of the nostril and lip.

The second proposition is amply demonstrated, as I have previously intimated, by the fact that the fluid contents of the accessory sinuses (chiefly antrum) may be absorbed by the lymphatic capillaries and carried to these contiguous glands. In confirmation of this view I can recall having seen a case of chronic, indurated lymph node of the cheek that had been diagnosticated sarcoma by several competent surgeons. It promptly and spontaneously disappeared after a nasal operation that restored antral drainage and free breathing. Whether this lymphoid hyperplasia was caused by a bacterial infection or by the absorption of an irritating lymph fluid was difficult to determine. That it was not sarcoma was convincingly demonstrated by its rapid and complete resolution.

I have previously noted the respiratory disturbances which have been present in the majority of the cases reported, and which require our careful consideration as ætiological factors. The relation of suboxidation and disturbed metabolism to these glandular enlargements is a vital one. My own cases showed marked interference with respiration and greatly lowered oxidation. Both patients were confirmed mouth breathers, and suffered from antral discharge. Excision of the tonsils removed the respiratory interference, and resolution of the enlarged glands quickly followed. Although Kümmel made a careful examination of nasal mucous membrane clippings in his case of hypertrophic rhinitis, the result of his study was negative. He was, nevertheless, greatly impressed by the clinical fact that whenever the nasal obstruction and asthmatic attacks become more pronounced a recurrence of the glandular swellings soon followed. Per contra, in my patients, involution of the enlarged glands was

promptly established as soon as the respiratory obstructions were removed. These are significant facts worthy of our most careful thought. The conviction is forced upon us that a careful examination of every case of Mikulicz's disease would probably reveal some lesion of the respiratory tract which had not been reported, either through inadvertence or through lack of special knowledge on the part of the observer.

Finally, we should bear in mind the ætiological element of hereditary or racial predisposition to lymphatic dyscrasiæ, which factor has been most pronounced in the cases so far reported in America, all of whom were members of the negro race.

PATHOLOGY.—The pathology of this disease is obscure. The histological picture has not been painted in the clearest colors, nor are the microscopic details as distinct as they should be. The macroscopical examination of the section of an extirpated gland made by Mikulicz showed enlarged normal gland structure imbedded in a loose mass of pale, yellowish red tissue of fatty consistency, but very poor in bloodvessels. The microscope revealed this mass to be an enormous infiltration of small, round cells into the interstitial tissue. In this mass were grouped the apparently unchanged acini, which seemed to be pushed or torn apart by the new tissue. In certain areas a portion of the normal gland had been choked out by the engorgement. I will quote Mikulicz's own pithy description: "The microscopical examination shows that the gland parenchyma proper plays a completely passive rôle. The enlargement is produced solely by the enormous small cell infiltration of the interstitial connective tissue." He asserts that the preservation of the capsule of the gland, and of the interlobular septa, forbid a diagnosis of typical sarcoma, the small cell infiltration histologically resembling most nearly the lymphadenoid tissue of true lymphoma.

Fuchs examined the nodular growths in his case and found the glandular elements absent, but the avascular texture of lymphoma present. Reymond's case showed lymphoid tissue with areas of amyloid degeneration. Adler found what he diagnosticated as small cell sarcoma, but complete resolution occurred under arsenic. The patient reported a "perfect cure" at the end of four and a half years, although he continued to take the arsenic for some

time as a preventive. Mikulicz pertinently remarks that this is not the usual behavior of sarcoma. In the case of Arnold-Becker there were dense accumulations of lymphoid elements imbedded in a delicate reticulum, with here and there a stronger connective tissue band, resembling completely a type of lymph follicle. These tumefactions were declared to be lymphadenomata. Power found hypertrophy of the interstitial web, but the gland substance was unchanged. Tietze noted entire absence of any glandular web, but the presence of a very spongy web of connective tissue, which was thickly permeated with small, round cells. Osler's case showed that the lacrimal glands had been replaced by fibrous tissue. No microorganisms were discovered in any of these cases.

Kümmel examined the salivary glands extirpated by Mikulicz and made a most elaborate report. Macroscopically he found them very soft, marrow-like in consistency, intensely white, and poorly vascular. The microscope showed a lymphoid trabeculum lacking in connective tissue fibres, imbedded with densely pressed round cells and lymphocytes poor in protoplasm. He formulated two alternative propositions: 1, The lymphoid proliferation may start at the acinus, the disease agent entering through the efferent duct of the gland, and forming a lymph follicle around the acinus; 2, the lymphoid web might also develop itself from the bloodvessels, this cell poor web thus representing the germinating centre. He later abandoned these theories as hypothetical, because of the slight evidence in their favor, and further acknowledged that the microscopical findings had often proved to be unreliable. He believed that lymphoma had an ectogenous origin, while leuchæmia and pseudoleuchæmia were hæmatogenous. He suggested that instead of leucocytosis of the lacrimal and salivary glands, the synonymous designation of "achroocytosis" should be adopted. As, however, this glandular enlargement is due to a lymphatic hyperplasia from leucocytic infiltration, I think we should accept the name "lymphoma" as more distinctly descriptive of this tumefaction.

Diagnosis.—The diagnosis of Mikulicz's disease should not be difficult. I have previously noted the characteristic facial appearance, consisting of ptosis of the temporal half of the upper eyelids, broad par-

otid swellings as in mumps, and tumefactions in the floor of the mouth. As the lacrimal and salivary glands are usually affected in pairs, the symmetrical character of their development should be emphasized as a diagnostic sign.

A differential diagnosis must be made between lymphoma and the glandular swellings of leuchæmia and pseudoleuchæmia. The freedom from the hæmic dyscrasiæ of the latter lesions, the nonparticipation of other lymph glands, and the absence of enlarged spleen, liver, or kidneys should decide the diagnosis in favor of lymphoma. Physical weakness, emaciation, and pyrexia are seldom present in a case of lymphoma, while total extirpation of the glands is not followed by recurrence. Enlarged tonsils are usually antecedent, and not developed synchronously, as may happen in pseudoleuchæmia. Petechia, hæmorrhage, and œdema are also manifestations of the latter disease. In the opinion of von Brunn, there is no reason for segregating diseases that are only distinguished by degrees. He believes that leucocytic infiltration of these glands is the first stage, leuchæmia the second stage, and pseudoleuchæmia the final stage of one continuous pathological process. This extreme view, however, is hardly sustained by the recorded facts, although there is some ground for his belief. We know that the blood picture presented by these radically divergent diseases, may vary from normal to almost complete disorganization. And yet the enlarged lacrimal and salivary glands seen in leuchæmia and pseudoleuchæmia show but little difference, either clinically or histologically, from the true lymphomata of Mikulicz's disease. The well known cases reported by Dunn and Derby typically illustrate the similarity of the facial characteristics. In fact, there are those who assert that a typical case of Mikulicz's disease can occur synchronously with these hæmic disorders, and, as it were, independent of them.

The malignant neoplasms may also complicate the diagnosis, especially lymphosarcoma. The microscopical examination of these glands has proved to be unreliable in several of the cases reported, the subsequent involution demonstrating the benign character of the tumor. This was notably true in Adler's case, where arsenic caused complete retrogression, in Mikulicz's case where the unoperated

tumors underwent resolution, and in the case of Frost, where one lacrimal gland was extirpated and the other disappeared spontaneously and permanently while awaiting the microscopic report of "sarcoma." Lymphosarcoma may or may not be bilateral, and is rarely primary in this location. It rapidly invades the surrounding tissues, spreads by metastasis, and when extirpated quickly recurs. Superficial cutaneous varicosities may form, and the skin may adhere and ulcerate. Carcinoma occurs but seldom, and is generally secondary to some initial growth elsewhere. It is usually nonsymmetrical, invades the surrounding tissues, and is accompanied by pain and cachexia.

Tuberculous adenitis can generally be excluded by Koch's tuberculin test. As a rule, the attack is not bilateral and other foci of infection may be found. Sooner or later there is a tendency to periadenitis, and suppuration may develop. Syphilitic adenitis can be differentiated by the history, the symptoms, and the therapeutic test. The glandular swellings may be unilateral. The additional evidence of enlarged cervical, epitrochlear, or inguinal glands will help to confirm the diagnosis.

These two diagnostic possibilities have probably interfered most with the isolation of this disease. Abadie and de Lapersonne were both dubious about the tuberculous origin of their cases. Osler first inclined to hereditary syphilis in his case, although there was neither interstitial keratitis nor dental notching present. Complete involution of the glands occurred during an intercurrent attack of pleurisy. The patient's death from tuberculosis two years later suggested a tuberculous origin, but the inference could not be substantiated. Posey's case was diagnosticated as hereditary syphilis, because it yielded to potassium iodide after a year's treatment. This does not necessarily confirm the diagnosis, as the same drug is useful in Mikulicz's disease. Stieren has reported an interesting case of supposed tuberculous dacryoadenitis which his own careful tests showed was absolutely free from tuberculous infection. These are all typical examples of Mikulicz's disease, occurring in negroes, and have been included in the reported list.

In rare instances the occurrence of lipoma of the lids has obscured the diagnosis. As both lids are usually involved, and the tumor is not so hard as

lymphoma, there should be no difficulty in differentiating this condition.

PROGNOSIS.—The prognosis is favorable, although the course of the disease is very chronic and liable to relapse. Some cases, like those of Adler and Bronner, have required continuous treatment for many years in order to maintain convalescence. Although the swollen glands may cause marked physical discomfort, no fatal issue has so far been reported.

TREATMENT.—The therapeutic agents that have been advocated in Mikulicz's disease are arsenic, the iodides, and pilocarpine. Of these, arsenic has had the greatest measure of success, the majority of cases yielding promptly to the internal administration of Fowler's solution. Many patients, however, are intolerant of its use in doses sufficiently large to influence this disease. Mikulicz, Adler, Axenfeld, Fuchs, Kümmel, and others have reported success in some cases and failure in others. Bronner records relief in his case, but a relapse when its administration was stopped. Its therapeutic value lies almost wholly in its ability to increase the oxidation of the blood, which, again, would suggest a certain underlying relationship between this disease and leuchæmia or pseudoleuchæmia.

The iodine preparations have been utilized successfully in some cases. Their activity depends upon an alterative effect on the lymphatic system, which in turn tends to increase the oxidizing power of the blood. Haltenhoff, Reymond, Horner, Scheffels and others report success in their cases from the use of iodide of potassium, and from syrupus ferri iodidi, the latter having been administered to children. Lugol's solution should exert the same specific action in this disease that it yields in exophthalmic goitre.

Pilocarpine has been employed by Mikulicz and others, but without marked success, notwithstanding the fact that it possesses a decided lymphagogue effect. Although apparently not as valuable as other remedies have proved to be, it should still be kept in mind as a therapeutic reserve.

In this connection the administration of thyreoid extract in small doses (gr.j to v, t.i.d.) should prove to be a most valuable therapeutic suggestion, as the disturbance in metabolism, the suboxidation,

and the katabolic stasis, all indicate the employment of such a remedy.

The tentative suggestion of Kümmel, that since intercurrent diseases cause retrogression of the enlarged glands it might be advisable to make an inoculation of such a disease for its therapeutic effect, does not merit our approval, as these results have not been permanent. All such cases of involution have shown recrudescence soon after convalescence was established, except those in which death intervened.

The application of the x rays has had a moderate degree of success in some cases. Fittig, von Brunn, Ranzi, and Pfeiffer have recorded good results from their use, while Cutler has noted their failure. Like arsenic, therefore, the x rays are useful in some cases, and of no value in others. I will quote Ranzi's views on this subject: "Next to internal medicines, we possess in the x rays an efficient remedy for the reduction of the gland tumors, as our case shows. This applies particularly to the parotids, where, as previously mentioned in the history, operative measures are contraindicated. A favorable influence of the x rays on the salivary and lacrimal gland tumors of Mikulicz's disease has previously been mentioned in only one case (Fittig). In the case treated by von Brunn, complicated with pseudoleuchæmia, the enlarged lymph glands were reduced to half their size by the x rays, but an irradiation of the salivary gland tumors was not attempted. It is not to be expected that the retrogression caused by the x rays means a lasting cure; in the course of years there were repeated small relapses in our case. But it always happened that the same shrinkage again occurred after short séances. This intense effect of the x rays on the described tumors corresponds entirely with their histological composition. We know, through the experiments of Heinecke on animals, as well as through the clinical knowledge of leuchæmia, that the x rays possess an elective action on the lymphatic tissues, and that very small doses lead to greater destruction of the lymphocytes. In the same way also in cases of Mikulicz's disease (which in their essentials resemble a local hyperplasia of the lymphatic tissues occurring normally in the salivary glands) the prompt involution of the gland tumors through irradiation can be explained."

Operative measures may be indicated in certain isolated cases. Extirpation of the enlarged glands has been practised by many, including Mikulicz, Kümmel, Gayet, and others, but not with any degree of success. Partial excision has been followed by renewed growth in the remaining portion, while total extirpation has been successful in preventing recurrence only because all glandular elements have been removed. The remaining glands have shown a more rapid growth on this account. We should bear in mind the important fact that the total destruction of these glandular functions may bring discomfort and possible disaster to the patient. On the other hand, if the glands are so large that their encroachment is distinctly harmful, then they must be extirpated. This, however, should only be considered as a *dernier ressort.* The operation of extirpation, especially of the parotids, is a difficult one, and often attended with considerable danger.

As previously pointed out, the usual treatment of this disease has for its objective aim the stimulation of lymphatic action and the increase of systemic oxidation. The correction of all obstructive respiratory lesions is, therefore, a therapeutic suggestion distinctly in line with this purpose. The fortunate results in my cases demonstrated this fact beyond a doubt. Respiratory obstructions should, on this account, be removed with promptness and good judgment, so that free nasal breathing may be quickly reestablished. Restoration of this physiological function tends to increase systemic oxidation, to encourage the evaporation of sinus secretions by the mechanical passage of the inspired air through the upper chambers of the nose, and to promote free drainage of the antrum. These retained fluids, as we have seen, may become either a nidus of bacterial infection or a cesspool of toxic secretions. Enlarged tonsils and adenoids should, therefore, be promptly removed, and swollen inferior turbinates should be reduced by linear cauterization, while obstruction of the upper air passage by a flabby or enlarged middle turbinate should call for its early excision.

Recapitulation.

In closing I desire to emphasize a few of the more important points by giving a brief résumé of the statements recorded in the paper.

1. Careful differentiation of the symptom com-

plex described by Mikulicz demonstrates that this disease is a pathological entity, *sui generis,* and not associated with any systemic disease.

2. The syndrome of symmetrical enlargement of the lacrimal and salivary glands is sufficiently characteristic to be accepted as pathognomonic of Mikulicz's disease.

3. The enormous lymph cell infiltration into the interstitial tissue, and the relative passivity of the gland structure, demand that this tumefaction shall be classed as true lymphoma or lymph tumor, as distinguished from adenoma or tumor of the glandular substance.

4. As no specific bacteria have been discovered, either in the glands or in the blood, the pathogenesis is probably chemotactic, thus causing a localized toxic hyperleucocytosis in the affected glands.

5. Toxic fluids that are chemically irritating are probably absorbed from the accessory sinuses (chiefly antrum) and transmitted through the lymphatic capillaries to these contiguous glands.

6. Respiratory obstruction not only hinders the evaporation and drainage of these sinus secretions, but also causes suboxidation and other disturbances of metabolism. It should, therefore, be considered a true ætiological factor.

7. The diagnosis of tuberculous adenitis and of lymphosarcoma has been repeatedly proved wrong by the spontaneous involution of the lymphomatous glands.

8. The glandular enlargements of leuchæmia, pseudoleuchæmia, syphilis, lipoma, and carcinoma are so characteristic that they should easily be differentiated.

9. The course of Mikulicz's disease is chronic, but the prognosis is favorable, with a tendency to relapse.

10. The treatment aims to improve lymphatic action and systemic oxidation. Arsenic, the iodides, pilocarpine, thyreoid extract, and the x rays have each shown some field of usefulness. All respiratory obstructions must be promptly and thoroughly removed. Extirpation is rarely indicated.

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