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FILAMENTARY KERATITIS*

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INTRODUCTION

Filamentary keratitis, Fädchenkeratitis, and keratitis filamentosa are terms used to describe a condition characterized by mild ocular irritation and the presence of small threads or filaments on the anterior surface of the cornea. The filaments can result from: (1) herpes of the cornea; (2) superficial injury to the cornea; or (3) destruction of the lacrimal glands.

This paper deals only with the latter condition, namely, those filaments resulting from destruction of the lacrimal glands. I will limit my discussion to those cases in which

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the lacrimal glands have not been destroyed by surgical intervention. My primary interest is to record a new form of therapy which gives great comfort to patients afflicted with this disease.

HISTORICAL BACKGROUND

1882—Leber[1] described for the first time the characteristic threads adherent to the anterior surface of the cornea.

1889—Fischer[2] reported several cases with filaments on the cornea.

1892—Hess[3] removed some filaments with a keratome and examined them histologically.

1893—Wagenmann[4] described a patient with "drying-up keratitis."

1900—Treacher Collins[5] sectioned a cornea showing filaments; he considered them to be the separating wall between two ruptured vesicles.

1903—Schirmer[6] reported his detailed studies on the physiology and pathology of the lacrimal gland, suggesting a method that gives a rough measure of the amount of secretion.

1919—A. Fuchs[7] reported the case of a woman with enlarged parotid glands and an absence of the salivary and lacrimal secretions. A suggestion was made that the condition was related to the menopause.

1924—Schöninger[8] reported two cases, calling attention to hypofunction of the lacrimal glands.

1927—Mulock Houwer[9] reported nine cases, associating five of them with arthritis and with normal lacrimal secretion.

1928—Albrich[10] described the pathologic changes in sections of lacrimal gland removed from three patients.

1928—Engelking[11] reported two cases, one of which was unilateral, following excision of the gasserian ganglion.

1928—Isakowitz[12] reported the association of the corneal filaments with a special form of arthritis, "peri-

arthritis of Umber," which he considered to be of endocrine origin (ovarian insufficiency).

1928—Betsch[13] published two more cases confirming the findings of Schöninger.

1929—P. Knapp[14] reported two cases occurring after surgical removal of the lacrimal glands.

1930—Schall[15] described 10 cases, all of which were relieved by *x*-ray therapy.

1930—Duke-Elder[16] reported a case of congenital absence of the lacrimal glands, and referred to the subject of dry eyes in general; his paper was entitled "Keratitis Sicca."

1931—Hauer[17] published the case of a woman who, when twenty-two years of age, a year following her third pregnancy, found herself unable to cry. From the age of fourteen years menses were normal, but became scanty following the inability to cry.

1933—Sjögren[18] published a comprehensive monograph on the subject of "Keratoconjunctivitis Sicca," in which he reviewed the literature in detail. His description of the disease was complete, and the histopathologic studies of the cornea, conjunctiva, and lacrimal gland were most thoroughly described.

Ocular Aspects of the Disease

Filamentary keratitis has been so adequately described by Sjögren as recently as two years ago that it is unnecessary to go into great detail here concerning some of its features. Nevertheless, in order to consider the etiology and to weigh a new form of therapy, we must briefly discuss the condition.

Ocular Symptoms.—These patients present symptoms of ocular irritation of varying degrees. Photophobia is somewhat constant. The eyes feel dry, and there is a burning sensation. A constant scratchy feeling is present, and the sensation as of a foreign body in the eye. Some patients complain of a stringy, thread-like mucoid discharge from

the conjunctival sac. Visual acuity is only slightly, if at all, impaired.

Ocular Findings.—The disease is always bilateral. There is circumcorneal injection of varying degree. A stringy, mucoid secretion is present upon the lid margins and in the conjunctival sac. One can usually see fine threads adherent to the anterior surface of the cornea; often they are just below the visual axis, in the part most exposed by the palpebral fissure. These threads or filaments vary in number—from 10 to 15 may be visible at one time. Between the filaments small, superficial defects in the epithelium occur; at times these are visible only with fluorescein, and often only with the aid of the corneal microscope. Occasionally one sees only the small corneal defects and no filaments. The filaments break loose from their corneal attachments when they are only a few millimeters in length; I have, however, seen one as long as 12 mm. The corneal surface appears to be dry, and the fatty secretions of the meibomian glands are visible upon it. There is a marked diminution in the amount of lacrimal secretion.

Frequency.—Filamentary keratitis is an uncommon disease. At the Massachusetts Eye and Ear Infirmary, where during the past seven years about 75,000 new patients were examined and some 300,000 additional visits made, such a condition was observed only five times; considered roughly, this is a frequency of 1 in 20,000. Zentmayer[19] called attention to the fact that he had seen only one case in twenty years of ophthalmic practice. Sjögren places the incidence at 1 in 2,000. Is it possible that the disease is 10 times as frequent in Europe as it is in the United States? Such may be the case, but, on the other hand, may it not be that observers in this country have failed to recognize such cases?

In addition to the five patients whose progress I have followed carefully at the Infirmary, there are four private cases to be reported, making a total of nine. Five of the nine cases will be dealt with very briefly (Table 1); the re-

maining four will be recorded in greater detail in case reports, as it is in these cases that this new form of therapy has been tried.

TABLE 1.—THE ETIOLOGY OF FILAMENTARY KERATITIS

Patient	E. H.	A. N.	M. S.	M. D.	F. W.	G. G.	H. K.	M. D.	K. M.
Present age	26	35	63	65	Died at 53	46	60	67	73
Age at onset	23	29	46	59	52	41	58	61	62
Lacrimation*: O. D. O. S.	5 3	5 9	2 2	Almost absent	Almost absent	3 3	5 6	Almost absent	Almost absent
Dry mouth	−	−	+	+	+	+	+	+	+
Enlargement of the salivary glands	+	−	+	−	−	+	−	−	−
Enlargement of the lymph glands	+	−	+	−	+	−	−	−	−
Enlargement of the spleen	+	−	−	−	+	−	−	−	−
Arthritis	−	−	−	+	0	−	0	+	+
Inadequate diet	+	+	+	0	+	−	0	+	0
Ovarian function: Abnormal menses Age at menopause Number of children	 − − 1	 − − 5	 − 48 married at 40 − 0	 − 49 1	 0 0 3	 − 43 3	 0 0 single	 0 0 2	 − 43 10
Basal metabolism	−3	+2	−20	0	0	normal	0	0	0
Wassermann reaction	−	−	−	−	−	−	0	0	0
Tuberculosis: Tuberculin Chest	 − −	 − −	 − −	 0 0	 0 −	 − 0	 0 0	 0 0	 0 0
Biopsy cervical glands	+	0	0	0	+	0	0	0	0
Biopsy lacrimal glands	+	+	+	0	+	0	0	0	0

Key: *Numbers indicate millimeters of moistening of strip of filter paper as described by Schirmer.
0 = No data available.
+ = Positive data available.
− = Negative data available.

Course.—The condition runs a chronic course, and there are periods when the ocular irritation seems to be worse. After considering the pathology of the disease, a complete cure would appear to be impossible. One must regard it as a permanent affliction. In four of the nine patients there was no lessening of the ocular irritation until the treatment I am about to describe was begun. Only one of the remaining five showed any lessening of the discomfort. I saw this

patient on two occasions only, and the information here recorded was sent to me in response to an inquiry two years later.

PATHOLOGIC STUDIES

The pathologic studies of this disease are well described by Sjögren, to whose article those who are interested are referred.

Cornea.—The epithelium presents some degree of keratinization. In certain places the superficial cells have desquamated. The filaments are threads of twisted epithelium, and, according to Sjögren, some of the threads are formed only of the outer cells and are extremely thin, whereas others arise from the entire thickness of the epithelium.

Lacrimal Gland.—Albrich described the changes occurring in small specimens of the lacrimal gland excised from three patients with this form of keratitis and Sjögren contributes many more such observations. Tissue removed from three of my patients showed similar changes. These changes consist of: (1) Round-cell infiltration of the gland structure of varying degrees. (2) Atrophy of the acini of the gland tubules. (3) Fibrosis. Similar changes may occur in the salivary glands.

GENERAL ASPECTS OF THE DISEASE: ETIOLOGY

That filamentary keratitis is a systemic disease there can be no doubt. Some of the patients complain of dry mouth, and are found to have an injected pharynx with a marked diminution in the amount of salivary secretion. An enlargement of the parotid gland has occurred in five of the 26 cases reported by Sjögren and myself. Generalized lymph-gland enlargement was observed in one-third of my cases. Arthritis was present in one-third of my cases, in two-thirds of those reported by Sjögren, and in five of the nine reported by Mulock Houwer. Inability to perspire was present in one case, and this may or may not bear some relation to the dis-

ease in general. Most of the cases occur after the age of forty, and the disease is found only in women, suggesting a relationship to ovarian dysfunction.

The various etiologic factors will be considered separately.

Lymphoma.—Three of my patients have had enlargement of the salivary glands, and although no enlargement of the lacrimal glands has been observed as yet, these patients would probably be classed in the literature as presenting a "Mikulicz syndrome." Mikulicz'[20] disease, as first described, was probably a lymphosarcoma. In this condition death may be expected within a reasonably short period of time. My patients have lived seventeen years, six years, and three years, respectively; it would seem, therefore, that we are not dealing with so malignant a disease.

A benign lymphoid tumor (lymphoma) cannot possibly be excluded. Three patients have had lymph-gland enlargement in one or more areas. In one case these enlargements disappeared within a short time following *x*-ray therapy; *x*-rays were not used for this purpose in the other two cases. In two cases a gland was excised for histologic study. In both instances the pathologist was unwilling to state whether the condition present was a lymph tumor or a chronic infection; but would prefer to say that it was the latter.

Numerous blood-smear examinations have failed to throw much light upon the subject, such differential counts usually being within the limits of normal. No increase in the leukocyte count has been observed.

Sections of the lacrimal gland show the lymph-cell infiltration and are compatible with lymphoid tumor formation, but on the other hand are neither suggestive nor conclusive.

Infection.—There is considerable evidence in favor of infection as a causative factor. We must assume that it is of low-grade virulence and chronic in nature, and, furthermore, that it has some specificity for gland tissue in general. An enlarged lymph gland has been removed from each of two patients for biopsy purposes. The pathologic report has been

most unsatisfactory, but in both cases it suggested a chronic inflammatory type of reaction. *X*-ray examinations of the chest have been made in four cases, and no pulmonary lesions have been found. Tuberculin skin tests were negative in three patients. Syphilis can be excluded with the negative blood serology in each instance. In three cases four-hour temperature charts were obtained for a reasonable length of time; these showed no elevation of temperature. Studies of the blood counts and blood smears have not been of assistance; one case showed a low white blood count a few weeks before death from peritonitis occurred. In reviewing the literature one is struck with the prevalence of arthritis. In only three of my cases was arthritis present. With this in mind, in two of the remaining cases, *x*-ray plates were taken which were negative. Histologic examination of the lacrimal gland is of no particular aid in determining the presence of infection, aside from the fact that there is marked round-cell infiltration present.

Avitaminosis.—The rôle of diet in this disease has scarcely been mentioned in the literature, but as one examines and studies microscopic sections, one is immediately confronted with the possibility of food being a factor. The epithelium of the cornea shows similar keratinization to that found in xerophthalmia. In both conditions, lacrimal secretion is known to be markedly diminished. Yudkin and Lambert,[21] in 1922, described lesions of the lacrimal gland produced in experimental xerophthalmia, consisting of mononuclear cell accumulations and foci of atrophy, and fibrosis in the animals that were cured. These observers conclude that "these changes account for some of the phenomena of xerophthalmia, particularly the drying of the cornea in the later stages of the disease." In other words, these changes resemble in all respects those found in the lacrimal glands of patients with filamentary keratitis.

It has been suggested[22] that the comparative frequency of the disease in Europe as compared with that in the United

States is explained on a nutritional basis. In five of my patients an inadequate diet could be held as a cause, but in each instance it was difficult to say that there was a definite vitamin deficiency. Several of these patients were on high vitamin diets over a considerable period of time, but none was appreciably benefited. This is not strange, however, when one considers that the pathologic changes that take place in the lacrimal gland would make it impossible for improvement in the form of increased lacrimal secretion to occur.

The theory advanced by Mellanby[23] in 1926 has been proved and disproved on many occasions. It contends that vitamin A has a definite anti-infective property. This would link avitaminosis with some infection, and the two together would explain the ocular changes found.

Pillat[24] has described a condition that he chooses to call "präxerosis," which is apparently due to lack of vitamin A, and which is not dissimilar to the condition which we are discussing here.

The other vitamins cannot be incriminated.

Hormone Dysfunction.—The literature contains two or three reports of filamentary keratitis occurring in males, but they are either inadequate or the cases do not belong to the group under discussion. This disease is essentially peculiar to the female sex. The 19 patients reported by Sjögren and the nine reported here were all of the female sex, and had an average age of fifty-four years. It would seem, therefore, that there must be some relation to a change occurring in the female during the menopause. This appears to be doubtful, however, when one studies the range of ages at the onset of the trouble, the youngest patient, twenty-three years, the oldest, sixty-two years. Several authors are of the opinion that the disease is due to an ovarian deficiency, but their evidence as to this is somewhat insufficient. Ovarian therapy has been used in several cases without resulting improvement, but one should not expect clinical improvement when

the pathologic changes present in the lacrimal gland are considered. Only one of my cases, Case 1, can definitely be associated with ovarian disturbance; in this case swelling of the parotid glands began when the patient was one month pregnant, and the irritable condition of the eyes set in during the puerperium. The seven patients who were married during the child-bearing age all had children. If sterility is taken as an index of ovarian function, one would say that there was no possible relationship between the latter and filamentary keratitis.

In three instances basal metabolism has been reported as normal. The only abnormal reading was in Case 3, in which the basal metabolic rate was −20. In this particular patient large doses of thyroid had no beneficial effect, either as regarded her eyes or her health in general.

The pituitary body has not escaped consideration. *X*-ray plates of the skull of two of the patients showed no enlargement of the sella turcica. No suggestion of acromegaly existed either in these cases or in those reported in the literature.

Neurotrophic Disturbance.—A consideration of the etiologic factors of this disease would not be complete without mentioning the possibility of neurotrophic disturbance. The lacrimal gland has a most adequate nerve supply: it is supplied by the trigeminal, the facial, and the sympathetic nerves. Blocking of the sphenopalatine ganglion, through which fibers from the facial nerve pass, will produce clinically a diminution in the lacrimal fluid at times. It is said[25] that section or destruction of either of these nerves can produce tear diminution. It must be admitted that, following destruction of its nerve supply, secondary atrophy of the gland could ensue, in which case we would find histologic changes in the gland such as we have described for this condition. We have no evidence, however, that this is the case.

Engelking[11] reports a case of ocular irritation and absence

of lacrimal secretion following extirpation of the gasserian ganglion. It is remarkable then that, with the frequency of this operation, more cases have not been observed following this procedure. Verhoeff[26] reports six cases of keratitis following gasserian ganglion operations; as all six showed marked diminution of lacrimal secretion, he was of the opinion that this was essentially an exposure keratitis. It is interesting to note that in this group of cases no definite filaments have been observed on the cornea.

The absence of lacrimation, the dryness of the mouth, and the inability to perspire led me at one time to the consideration of a generalized disease of the sympathetic nervous system. A sympathectomized patient would show the same symptoms. No such disease is known to exist.

Corneal sensitivity is usually normal, but it may be slightly diminished. With the slit-lamp no abnormality of the corneal nerve fibers can be observed.

CLINICAL STUDIES

1. *Measurement of the Amount of Lacrimal Secretion.*— A rough measurement of the amount of lacrimal fluid secreted can be obtained in the manner described by Schirmer.[6] A piece of ordinary filter paper 5 mm. in width and from 25 to 30 mm. in length is employed. One end is inserted into the conjunctival sac at the inner canthus, covering the lower punctum; the other end is free and hangs down over the cheek. The lacrimal secretion that is present is absorbed by the filter paper, and the measurement of the length that the strip is moistened in a given length of time is an indication of the amount of tearing. In the case of a person with normal lacrimal secretion the strip will usually be moistened for a length of more than 15 mm. within five minutes. I have used this method on many patients with normal eyes, and on several occasions the measurement has been as low as 10 mm. A distance of less than 10 mm. in five minutes would signify, therefore, diminished lacrimal secretion. This

method was used in most of the cases here mentioned, and it will be seen that tearing was reduced to a marked degree.

2. *Efforts to Increase Lacrimal Secretions.*—A few of these patients have been subjected to various procedures in an effort to produce irritation or reflex stimulation of the lacrimal gland. Sjögren discusses this subject in detail, giving a table showing his observations. The methods employed include:

1. Bringing onion vapor near the eyes.
2. Placing ammonia vapor near the nose or eyes.
3. Bringing formalin near the nose or eyes.
4. Blowing smoke directly into the eyes.
5. Gentle irritation of the nasal mucous membrane by means of a brush.
6. Touching the cornea with a hair or a foreign body.

These procedures are followed by little if any noticeable increase in the amount of lacrimal secretion. Sjögren found an increase in a few patients, but in most cases there was very little tendency to produce a greater quantity of secretion. Tear gas has not been tried. Large injections (subcutaneous) of physostigmin failed to produce any increase of lacrimation, salivation, or perspiration in one patient on whom they were tried.

THERAPY

Before the pathologic changes in the lacrimal gland were recognized, this form of keratitis was treated locally with various ointments and eye-drops. Symptomatic treatment was indicated to relieve the discomfort of such patients. Mild anesthetic drops or ointments would seem to be necessary to relieve the burning and ocular irritation; holocain, butyn, pantocain, tincture of opium—one-half strength, and even cocain have been used for this purpose, but each has given but temporary relief. Because of the drying of the cornea, ointments of various kinds would seem to be of value. To provide additional moisture to the eye, Dr.

Verhoeff suggested the use of an ointment saturated with Ringer's solution. This has probably been of more value than any other form of medication, but here again very little relief is obtained, and the use of the ointment is soon discontinued by the patient.

Internal medication has had a prominent place in the treatment and has assumed many forms. Potassium iodid, ovarian extract, thyroid extract, and diets rich in vitamins have been suggested and have been used without any apparent improvement in either the ocular or the general condition.

In this disease the lacrimal gland contains lymph cells in great abundance, and it would seem that exposure of the gland to deep radiation in the form of the *x*-ray would destroy this type of cell. If such a gland were exposed to these rays before the tubules had been destroyed, some definite improvement might be expected to follow.

It has been stated that the *x*-ray, applied in small doses, will stimulate the secretion of the remaining gland tissue, and that large doses will inhibit it. Both dosages have been tried on two patients without any apparent change in the amount of secretion occurring. Two patients have also had their parotid glands exposed to the *x*-ray; one noticed no change, since she did not complain of lack of saliva; the other patient had a very dry mouth, and irradiation of the parotid glands did not increase the amount of saliva, although in both cases the parotid enlargement rapidly subsided. Even if some stimulation of the secretion should occur following such therapy, it would seem to me that it would be very temporary in nature. *X*-ray treatment probably destroys the lymph-cell infiltration, and fibrous-tissue proliferation is then made easier. I cannot understand the results obtained by Schall,[15] who reports success in the 10 cases treated in this manner.

The lacrimal gland tissue has been destroyed, and unless regeneration of this tissue can be effected, one should not

expect a permanent increase in the amount of lacrimal secretion. There is no evidence as yet that lacrimal gland tissue regenerates. Assuming that these irritable eyes are entirely the result of a lack of tears, we find ourselves considering the possibility of making better use of the tear supply that is available. Although lacrimal secretion is markedly diminished, fortunately it is never completely absent. The mechanism of the flow of tears into the naso-lacrimal duct is not clearly understood, but with the idea in mind that these ducts might be functioning in spite of the diminished amount of secretion, I decided to destroy them and note the effect. In other words, by destroying the conductivity of these ducts, I hoped it would be possible to make better use of the tears that were formed by the atrophied lacrimal glands.

Eight eyes have been treated by this method, and in each instance the improvement has been immediate and remarkable. Filaments are no longer visible on the cornea; the fine superficial staining areas are markedly diminished in number; the mucoid conjunctival discharge is absent; the pericorneal injection has disappeared, and photophobia is no longer annoying. This is the result of the increase in the amount of lacrimal secretion present in the conjunctival sac. In every instance the measurable amount of secretion was increased, and there can be little doubt but that the increase was produced by the obstruction to the natural drainage into the naso-lacrimal ducts.

It can safely be said that patients with filamentary keratitis have no use, and never will have, for their canaliculi, and destruction of the latter can therefore be considered a harmless procedure. Various methods of effecting this have been advocated, but only two have been tried. Cauterization of the puncta with the actual cautery seemed to be the simplest procedure and was the first to be carried out. Two weeks after vigorous cauterization of the puncta they were found to be wide open. They were cauterized again in a similar manner, and again healing occurred with the puncta being

left patent. It seemed to me, therefore, that more than the puncta alone should be destroyed.

TABLE 2.—FILAMENTARY KERATITIS—REGARDING TREATMENT

	*Tearing**		*Remarks*
	O. D.	*O. S.*	
CASE 1....	5	3	Before treatment.
	dry	moist	Two weeks after cauterization puncta, O. S.
	dry	dry	Six weeks after cauterization puncta, O. S. Puncta found to be patent.
	8	14	Two weeks after recauterization puncta, O. S.
	5	8	Eight weeks after recauterization puncta, O. S. Puncta again found to be patent, but not so large as in O. D.
	12	12	Six months after puncta and canaliculi of both eyes apparently destroyed with diathermy.
CASE 2....	5	9	Before treatment.
	27	2	One month after puncta and canaliculi, O. D., apparently destroyed with diathermy.
	12	12	Two months after puncta and canaliculi, O. S., apparently destroyed with diathermy. Three months after puncta and canaliculi, O. D., apparently destroyed.
CASE 3....	2	2	Before treatment.
	3	15	One week after puncta and canaliculi, O. S., apparently destroyed with diathermy.
	16	12	Two weeks after puncta and canaliculi, O. D., apparently destroyed with diathermy. One month after puncta and canaliculi, O. S., apparently destroyed.
	8	8	Two and one-half months after puncta and canaliculi of both eyes apparently destroyed with diathermy. Puncta all patent but openings somewhat small.
CASE 4....	3	3	Before treatment.
	13	12	Three weeks after puncta and canaliculi of both eyes apparently destroyed with diathermy.

* Numbers indicate the millimeters of moistening of the strip of filter paper as described by Schirmer.

The usual ophthalmic diathermy current was next considered. An electrode having the diameter of a No. 3 lacrimal probe was scraped free from insulating material for a length of 2 cm. This electrode was then inserted into the punctum and canaliculus as far as the lacrimal sac; a current of from 40 to 60 milliamperes was used for a period of from two to three seconds. In three instances the destruction so

produced has apparently been permanent; in the other patient the destruction was insufficient and will probably have to be repeated. Tying off of the canaliculi has been considered but never attempted. Extirpation of the lacrimal sac would be an excellent procedure, but a simpler operation would work as well. I would, therefore, suggest the use of the diathermy current for this purpose, but the method by which this destruction is effected is really of little importance. It is imperative, however, to make sure that the destruction of the canaliculi and puncta has been complete and will be permanent.

CASE REPORTS

CASE 1.—Mrs. E. H., aged twenty-four years.

1933, May and June: The patient was admitted to the Massachusetts Eye and Ear Infirmary and later to the Massachusetts General Hospital for study.

History.—Painless swelling of parotid glands fifteen months previously when patient was one month pregnant. Pregnancy was uneventful and child was delivered seven months ago. Since then eyes have been irritable, with slow increase of discomfort up to the present time; sensation as of sand in eyes, marked sensitivity to light, and some injection. The patient was unable to cry, although at times felt like doing so. No soreness of the mouth was present, but she believed that the mouth was somewhat dryer than formerly. Menses had been regular and normal previous to pregnancy. She had never been ill except for influenza fifteen years ago. There was no history of any familial disease. There was no abnormal dietary history, although the patient had been subsisting on only a few dollars a week. She had lost 20 pounds in weight since her marriage two years previously.

Findings.—Marked photophobia and moderate circumcorneal injection were present. There was considerable diminution of tears: Schirmer's test read 3 mm. O. S., 5 mm. O. D., in five minutes. There were many small superficial corneal defects, and numerous small filaments were adherent to the corneal surface; the condition was worse in the left eye. The corneal sensitivity was apparently normal. There were enlargement of the lymph glands and splenomegalia, and enlargement of the parotid and submaxillary glands. The physical examination was otherwise negative.

Laboratory Data.—Uripalysis negative. Blood count: white, 10,000; red, 4,190,000. Hemoglobin, 80 per cent. Smear: moderate achromia; polymorphonuclears, 54 per cent.; lymphocytes, 43 per cent. Hinton test negative. Tuberculin skin test negative in dilution 1/1000. Basal metabolic rate, −3. *X*-ray examination of chest negative. Four-hour temperature chart of three weeks' continuity showed no elevation.

Procedures.—(1) Tight goggles were prescribed, in the hope that by this the drying of the cornea would be lessened, and the patient be more comfortable. They were worn for a period of one week, with little if any relief. (2) A contact glass was applied, in the hope that the normal saline solution between the glass and the cornea would lessen the irritation. The glass was tried for thirty-six hours; the patient was rendered very uncomfortable and was anxious to have it removed. (3) Biopsy of cervical and axillary gland. (4) Biopsy of lacrimal gland.

Pathologic Report.—Cervical and axillary glands: "Hyperplasia; unable to diagnose lymphoma on tissue submitted." Lacrimal gland: "Destruction of acini, fibrosis, and small round-cell infiltration."

Diagnosis.—Probable lymphoma with Mikulicz syndrome.

1933, July: Lacrimal puncta, left eye, cauterized with actual cautery.

1933, August: Patient reported that the left eye was much more comfortable and that now the right eye was worse than the left. There was visible lacrimation in the conjunctival sac. The epithelial defects were less marked; no filaments were present.

1933, September: Generalized *x*-ray therapy was begun for treatment of the lymph gland enlargement and parotid swelling.

1933, October: The left eye had been very comfortable until two weeks previously; since then there had been a return of the previous irritation. Both puncta were found to be open and patent. Lacrimal puncta, left eye, were recauterized with the actual cautery.

1933, November: The eyes were again fairly comfortable, especially the left eye. Lacrimation as measured by Schirmer's test: 8 mm. O. D., and 14 mm. O. S. The cornea of the left eye had fewer staining areas than that of the right; no filaments were visible in either eye.

1934, January: The eyes were again more irritable. All the puncta were patent, but those of the right eye were larger than those of the left. Tearing: 5 mm. O. D., 8 mm. O. S. Fine superficial staining areas were present on the corneas in considerable numbers.

1934, February: The lacrimal puncta and canaliculi of both eyes were destroyed by electrocoagulation.

1934, June: The eyes were quite comfortable. Tearing: from 10 to 12 mm. in both eyes. With the corneal microscope a rare minute staining defect was noted.

CASE 2.—Mrs. A. N., aged twenty-seven years.

1929, October: The patient was examined in the Massachusetts Eye and Ear Infirmary Outpatient Department. She complained of ocular fatigue. She was found to have normal eyes, with a visual acuity of 6/6 in each eye.

1931, July: The patient returned to the Infirmary complaining of discomfort in the right eye of several days' duration. She was seen by a clinical assistant and no pathologic changes were noted.

1932, July: The patient had had constant discomfort in the right eye. She was seen by the same clinical assistant and no pathologic changes were noted.

1933, January and February: The patient was admitted to the Massachusetts Eye and Ear Infirmary for study.

History.—Ocular discomfort of the right eye of one and one-half years' duration. The patient was unable to cry, although she felt like crying at times. There was no complaint of lack of saliva. Her husband had died three years previously; there were five pregnancies before that time. Menses were regular. Her diet was inadequate, although no definite vitamin deficiency was noticeable. She had lost 20 pounds in weight during the past two years.

Findings.—Slight photophobia was present. Fine filaments were adherent to the corneas; these were seen best with the slit-lamp. There was a marked diminution in the lacrimal secretion. Visual acuity equaled 6/6, each eye. The tongue was smooth and pale. There were no palpable lymph glands. The physical examination was essentially negative.

Laboratory Data.—Urinalysis negative. Blood count: red, 3,410,000. Smear: slight achromia; normal platelets; polymorphonuclears, 63 per cent.; lymphocytes, 25 per cent.; eosinophiles, 8 per cent. Hinton test negative. Basal metabolic rate, +2.

Procedure.—(1) Tight goggles were prescribed, and no particular relief was obtained, as in Case 1. (2) High vitamin diet prescribed.

1933, July: The symptoms continued unchanged. The patient complained of distress in both eyes, but more severe in the right eye. There was marked suppression of tear secretion. Biopsy of lacrimal gland.

1933, August: Filaments were present on both corneas. Tear

secretion: 7 mm. O. D., 8 mm. O. S. Thyroid extract, 1½ grains daily, was prescribed. The high vitamin diet was continued. In an effort to stimulate secretion, as recommended by Schall, the patient was referred for *x*-ray therapy of the right lacrimal gland region.

Pathologic Report.—"Section of lacrimal gland shows some atrophy of glandular structure, fibrosis, and small round-cell infiltration."

1933, October: Last of *x*-ray treatments, of which there were six. Tear secretion: 5 mm. O. D., 9 mm. O. S. Destruction of puncta and canaliculi, right eye, with electrocoagulation.

1933, November: Marked improvement was noted; patient was more comfortable. Tearing now 27 mm. O. D., and 2 mm. O. S. A few superficial corneal staining areas were present in the right eye; many more were observed in the left eye. Destruction of puncta and canaliculi, left eye, with electrocoagulation.

1933, December: Both eyes were moist. Corneal defects were practically gone.

1934, January: Eyes were comfortable. No staining of corneas was present. Tearing: 12 mm. in both eyes.

1934, September: Eyes were moist. Patient was comfortable.

CASE 3.—Mrs. M. S., aged fifty-six years.

1928, November and December: The patient was admitted to the Massachusetts Eye and Ear Infirmary for study.

History.—The left eye had been irritated for ten years; the right eye for about four years. The eyes were dry, and the patient was unable to cry. The mouth and throat were dry and very uncomfortable. There was inability to perspire. The menses had been regular, the menopause occurred at forty-eight; there had been no pregnancies; she had married at the age of forty. She had had an abdominal operation at the age of thirty, the exact nature of which was unknown. She had been extremely nervous and miserable since the death of her husband, six months ago. There was no familial disease and no serious illness in her past history. The patient had consulted many oculists and general physicians, who had prescribed eye-drops, ointments, and internal medicines, without resulting relief.

Findings.—Many fine, superficial staining areas were observed on each cornea. Numerous filaments were adherent to the anterior surface of each cornea. There was slight ciliary injection. The conjunctiva was dry, with practically no lacrimal secretion. A stringy, mucoid epithelial secretion was present in the conjunctival

sacs. There was a high degree of myopia present, and corrected visual acuity of 6/12 both eyes. There was no evidence of salivary or lymph gland enlargement. The tongue and pharynx were dry and red. The physical examination was essentially negative.

Laboratory Data.—Urinalysis negative. *X*-ray examination of the hands and head were negative. Basal metabolic rate, −13.

Procedure.—(1) Large subcutaneous injections of physostigmin failed to increase salivation, perspiration, or lacrimation. (2) Large doses of potassium iodid had no effect on salivary or lacrimal secretion. (3) Ovarian extracts of various kinds had no noticeable effect upon the patient's symptoms. (4) Slight improvement was temporarily brought about by the use of an ointment containing salts, according to the formula of Ringer.

1929, July: The patient was admitted to the Massachusetts General Hospital for study.

Interval History.—A recent painless swelling was noted in the region of the right parotid gland. The eyes and mouth were just as uncomfortable as previously—*i. e.*, no change had occurred during the past six months.

Findings.—Enlargement of the right parotid gland. The physical examination was otherwise negative. The ocular appearance was the same as it had been.

Laboratory Data.—Basal metabolic rate, −20. Gastric analysis negative. Wassermann reaction negative. Blood count: white, 6,900; red, 5,300,000. Hemoglobin, 90 per cent. Smear: polymorphonuclears, 75 per cent.; lymphocytes, 24 per cent.; no achromia.

Diagnosis.—The patient was examined by various members of the staff, but no satisfactory diagnosis was reached. Such possibilities as psychoneurosis, endocrine dysfunction, avitaminosis, lymphoma, and disease of the sympathetic nervous system were considered.

Procedure.—*X*-ray therapy was applied to the parotid gland.

1932, March: The patient was readmitted to the Massachusetts General Hospital for study.

Interval History.—Swelling of the left parotid region had been present for the past six to twelve months. Three years ago the swelling of the right parotid had subsided within two months following *x*-ray treatments. The eyes remained as uncomfortable as ever.

Findings.—Enlargement of the left parotid gland. Enlargement of the lymph gland in one axilla. Ocular appearance the same as before.

Procedure.—Biopsy of lacrimal gland. *X*-ray therapy applied to lacrimal gland.

Pathologic Report.—Lacrimal gland: "Lymphocytic infiltration around acini of gland. Acini greatly reduced in number."

1934, November: The patient was readmitted to the Massachusetts General Hospital for study.

Interval History.—The eyes had remained uncomfortable. The mouth had been as dry as ever. During the past three years there had been slowly progressive enlargement of the left parotid gland. The patient complained of dizziness, fullness in the head, and tinnitus. No medication of any kind had been administered during the past three years.

Findings.—Marked enlargement of the parotid gland. Many filaments were present on both corneas. Tearing less than 2 mm. in both eyes. Marked ocular irritation.

Procedure.—Lacrimal puncta and canaliculi, left eye, were destroyed with electrocoagulation. *X*-ray therapy to parotid gland.

1934, December 1: There was marked relief from the irritation in the left eye. No filaments were present. Very few small staining areas were noted on the cornea. Mucoid secretion was absent. Tearing: 15 mm. O. S., 3 mm. O. D. The patient desired the right eye to be treated in a similar manner. The lacrimal puncta and canaliculi of the right eye were destroyed with electrocoagulation.

December 6: Eyes were comfortable. Tearing: 16 mm. O. D., 12 mm. O. S. No photophobia. No injection. No stringy, mucoid discharge.

1935, February: The eyes had been fairly comfortable for the past two months, but not quite so good now as they were one month ago. Tearing: 8 mm. in both eyes. All the puncta appeared to be patent, although the openings were quite small. They will probably need more thorough destruction later. The parotid swelling was gone, but the mouth was as dry as ever.

CASE 4.—Mrs. G. G., aged forty-six years.

1934, December: The patient was incompletely studied.

History.—The eyes had been irritable for the past five years. Much stringy discharge was present in the eyes; she was unable to cry. The mouth was dry and uncomfortable. Menses were regular; she had had three children; the youngest being eleven years of age. The patient had had excessive menstrual flow three years ago, and a hysterectomy was performed at that time. She had consulted many physicians without obtaining relief from the inflamed eyes

and dry mouth. She had been on a high vitamin diet for many months.

Findings.—There was enlargement of both parotid glands. No lymph gland adenopathy was noted. Filaments were present on both corneas; many fine superficial staining areas were observed. Tearing: 3 mm. in both eyes. Much stringy, mucoid conjunctival secretion was present. There was congenital heterochromia iridis, with no evidence of iridocyclitis. Visual acuity, O. D., 6/12; O. S., 6/7, with correction.

Procedure.—The lacrimal puncta and canaliculi of both eyes were destroyed by electrocoagulation. *X*-ray therapy to parotid glands was suggested, but the patient was unwilling to accept it at that time.

1935, January: The patient was much more comfortable. No filaments were present on either cornea. With the slit-lamp no staining defects were visible. Mucoid conjunctival secretion was absent. Tearing: 13 mm. O. D., 12 mm. O. S.

SUMMARY

Patients with filamentary keratitis present an interesting medical problem. Attention is again called to the following: (1) There are infiltration, atrophy, and fibrosis of the lacrimal and salivary glands; (2) there are various degrees of ocular irritation and filament formation on the corneas, the direct result of desiccation due to insufficient lacrimal secretion. Various possible etiologic factors have been considered; some hormone dysfunction is undoubtedly a basic factor. A new form of therapy for such patients has here been described, which consists of destruction of the canaliculi in an effort to utilize to good purpose the small amount of lacrimal secretion which characterizes this disease.

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EXPERIMENTAL UVEITIS: "INTERFERENCE" EFFECT OF PARENTERAL ADMINISTRATION OF PROTEINS ON SENSITIZATION OF THE UVEAL TRACT*

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The parenteral administration of various proteins in the treatment of uveal tract inflammations is an established procedure. The theories regarding the action of nonspecific proteins are based on the interpretation of various reactions accompanying their use. These reactions fall grossly into two classes. The first class includes the general reactions of increased temperature, leukocytosis, and an occasional increase in the normal serum complement. The second class concerns the production of specific antibodies following protein injection, and the concomitant stimulation of relatively nonspecific antibodies. The general reactions have led Weichardt[1] to assume that the essential mechanism is one of universal stimulation of the body cells to greater

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