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THE PROGNOSIS OF TUBERCULOUS LARYNGITIS*

BY

F. R. G. HEAF, M.D.

MEDICAL SUPERINTENDENT, COLINDALE HOSPITAL

I must ask for the acceptance of my conclusions as those of a phthisiologist who has taken a special interest in the changes of the larynx in tuberculous patients for a number of years, and for a review of them in the light of the wider knowledge and experience of oto-rhino-laryngologists. It would seem at first that the answer to the question "What is the prognosis of tuberculous laryngitis?" could be answered by the single word "bad"; some might require to qualify it by saying "very bad." Why then spend time in discussing a subject apparently so dismal and depressing? The reason is that there are few diseases in which such important changes in treatment and prognosis have taken place during the last few years as in tuberculosis, and these changes have materially affected the outlook on one of the most serious complications of the infection. Nowadays far more attention is paid to the larynx in tuberculous patients, with the result of earlier diagnosis, better response to treatment, and a more favourable prognosis.

THE POSITION THEN AND NOW

Forty years ago tuberculous laryngitis was regarded as absolutely incurable. Sir StClair Thomson gives a number of quotations in his masterly survey of tuberculosis of the larynx, published in the Special Reports of the Medical Research Council.¹ Three of these illustrate the pessimistic view prevalent fifty years ago. In 1880 Morell Mackenzie² wrote: "It is not certain that any cases ever recover." In 1894, Lennox Brown³ reported one case in which cure had been effected, and at that time Kreshaber of Paris wrote of tuberculous laryngitis that it "invariably ends fatally."

In some respects the general opinion of the prognosis of tuberculous laryngitis has not changed very much since those days. Standard textbooks on medicine still contain phrases such as: "It is doubtful if any cases of extensive infiltration recover, with exception of a few rare instances where it is confined to the epiglottis and can be

entirely removed." The infected larynx is still regarded as the certificate of death by the majority of clinicians, but the patient and his relatives rarely regard the complication as serious. This is to some extent fortunate, in that the patient is stimulated by an unfailing hope that his symptoms can be relieved and a recovery secured. This optimism does play an important part in the prognosis of the lesion, for if it fades away and is replaced by despondency treatment will then be of little avail and the result will be disastrous. Unfortunately there is a tendency for an excess of assurance to lead to complete disregard of advice—particularly with reference to resting the voice—thereby endangering the future.

The pessimistic attitude towards tuberculous laryngitis is greatly due to the fact that the complication is usually associated with advanced pulmonary lesions, and in a large number of cases is first diagnosed when the lungs have become grossly infiltrated. Further support to this impression is given by the statistics compiled by observations made at necropsies on patients dying from pulmonary tuberculosis. Fetterolf, quoted by Spencer,⁴ found the larynx involved in eighty-three out of a series of 100 cases, and in a series of 150 necropsies on my own cases I found the larynx involved in 68 per cent. Of this 68 per cent. I found 44 per cent. had ulceration of the intestines, a figure which is of importance, as there seems to be some connexion between the two complications. It will be seen that over two-thirds, maybe over three-fourths, of cases suffering from pulmonary tuberculosis have laryngeal infiltration before they die. It is thus easy to conclude that if a pulmonary patient develops laryngitis then his days are numbered, and the end is not far off. Now if this were true how sad and depressing would be the work of a laryngologist in a tuberculosis hospital or sanatorium! Can one imagine anything more hopeless and melancholic than passing a death sentence on men and women by diagnosing an incurable condition which will end their days in the near future?

Happily such a conclusion, based merely on observations made in the post-mortem room, is not true. Because the majority of patients dying from pulmonary tuberculosis suffer from active laryngeal infiltration it does not follow that a patient with laryngitis is bound to die from pulmonary tuberculosis, or that the laryngitis determines the fatal termination of the disease. There is evidence that a patient with pulmonary and laryngeal tuberculosis can recover completely from the laryngitis and yet succumb to the chronic pulmonary lesion. I had two such cases in my series, and Cooper and Benson⁵ report thirty-nine from a series of 798 necropsies on pulmonary cases. If the larynx can recover in patients actually dying from pulmonary tuberculosis, to how much greater an extent can we expect recovery when the pulmonary lesion is also arrested?

FACTORS IN PROGNOSIS

We have met to-day to determine the factors and conditions which influence the possibility of recovery from the laryngeal lesion, and I will now ask you to consider the most important points which control the prognosis of this interesting subject. I say "interesting subject" because, during the fifteen years I have been examining the throats of tuberculous patients, I have learnt the extreme value of this procedure, by which one can gain information in many cases of the patient's resistance to the disease, of his temperament, of his symptoms, and occasionally of his habits, by a laryngeal examination. The prognosis of tuberculous laryngitis depends on all these factors, and many more, for although the nature, position, and extent of the local lesion must be considered, the most important information is the amount of resistance the patient has to the disease.

* Read in opening a discussion in the Section of Oto-rhino-laryngology at the Annual Meeting of the British Medical Association, Dublin, 1933.

To determine this we must review the previous history, especially the rapidity of onset of the disease, the family history, and the type of pulmonary lesion. The laryngologist has often to depend on the physician for this information, but if we can assess the degree of resistance ourselves so much the better. I should like particularly to emphasize the importance and value of a blood examination in making this assessment, more especially the value of two observations made under similar conditions at intervals of a few weeks whilst the patient has been under treatment. A serial blood examination will sometimes reveal the true state of the patient's condition when all other evidence makes us tend to form an opposite opinion. The combination of (1) a rapid sedimentation rate, (2) a high monocyte count, and (3) a low lymphocyte and eosinophil count, which does not show any tendency to change, means a poor resistance, and so long as that state continues the laryngeal lesion will not improve.

Closely connected with the patient's reaction to the infection is the type of lung lesion. A study of this will help in the formation of an opinion on the larynx. Generally speaking, the more fibrotic the pulmonary condition the less severe is the laryngeal activity. The case with large areas of soft caseous or pneumonic disease—the exudative type—will develop an active oedematous type of laryngeal lesion which rapidly ulcerates, and is difficult to control, whereas laryngitis in a fibroid case is generally of a benign character, very slowly progressive, responding to treatment rapidly, and having little or no influence on the general progress of the case.

As fibroid phthisis is more frequent in patients over 40, and the general resistance to the infection increases as age advances, we find that the consequence of tuberculous laryngitis becomes less and less important the older the patient becomes. I have been struck by the high percentage of complete recoveries one obtains in men over 40. Out of a series of 110 cases definite arrest of the laryngeal lesion, with complete disappearance of symptoms, was obtained in 25 per cent. of men over 40. The predominating type of laryngeal lesion in the cases in which a good result was obtained was an infiltration, showing congestion but little oedema, and very rarely any ulceration.

TYPE OF LESION IN PROGNOSIS

This brings me to the discussion of the character of the lesion as a guide to the prognosis. Naturally the small lesion has, in most cases, a better chance of recovery than the extensive one, although occasionally we come across patients with little or no resistance in whom the laryngeal lesion is diagnosed in a remarkably early stage, and yet, in spite of most thorough treatment, progresses to panoedema with extensive ulceration. Omitting this type, I have made four classes for the purpose of prognosis.

1. The extrinsic { ulcerative.
non-ulcerative.
2. The intrinsic { ulcerative.
non-ulcerative.
3. The localized lesion { ulcerative.
non-ulcerative.
4. The lupoid { ulcerative.
non-ulcerative.

Each class falls into two subdivisions for ulcerative and non-ulcerative cases. A generalization may be immediately made by stating the obvious—that the prognosis is better in the non-ulcerative than in the ulcerative type—but it must be remembered that the position of the ulcer has some bearing on the future of the case.

The first class includes the aryteno-epiglottic cases, with massive infiltration, oedema of the epiglottis, and pyriform swelling of the arytenoids. The cords may be

clear even in the last stages. The prognosis in these cases is very bad. In the young adult up to the age of 30 it is hopeless. After 40 they respond moderately to treatment, but the improvement is not permanent. The lesion nearly always shows signs of ulceration, and the length of life is almost indirectly proportional to the area of ulceration. The second type comprises cases with corditic and inter-arytenoid infiltration. Here the prognosis is comparatively good, partly owing to the general absence of dysphagia and the good response to rest treatment. If, however, the infiltration extends to the arytenoids or the ventricular folds, the possibility of recovery is reduced by about 50 per cent. An important symptom in determining the future of these cases is that of dysphagia. Whilst this symptom is absent I always feel that there is some hope of recovery, and, roughly speaking, so long as the infiltration is not markedly oedematous, and is confined to the inner ring of vocal cord and inter-arytenoid fold, a response to treatment is probable, but when the outer ring of epiglottis and arytenoids is mainly the site of the lesion the case has a most unfavourable outlook.

A certain number of cases do not fall into these two classifications, and I place some of them in the category of the localized type. In these cases the lesion is nearly confined to one side of the larynx, or localized to two small areas on either side. It may be one cord, an arytenoid, or one side of the epiglottis, or a combination of these. There may be some inter-arytenoid thickening, but so long as the infiltration leaves half the larynx clear and healthy, or is localized to one particular area, I place the case in this class. I make this division because I have found the majority of the cases do very well, particularly if little or no ulceration is present and the lesion is characterized by firm infiltration.

Lastly, I come to the lupoid type, in which I include the granular, papillary, and smooth, defined tuberculo-mata. They rarely cause symptoms, respond most favourably to treatment, and do not affect the general prognosis of the case to any appreciable extent.

We will now consider the prognosis, with reference to the unusual sites of the early lesion, and their direction of spread. The most frequent order of involvement is the arytenoid, the inter-arytenoid fold, the vocal cords, the ventricular bands, and the epiglottis. The most favourable site of onset is the vocal cords, and after that the inter-arytenoid region. With localized lesions the prognosis is good, particularly if the infiltration is of the firm, fibroid type. One need not be unduly pessimistic about a hard, localized swelling over a moderately large area, but if there is oedema present, especially if it is accompanied by ulceration and necrosis of the tissues, there is usually a distressing amount of dysphagia, and the future becomes extremely grave. Solitary lesions on the vocal processes are not uncommon. They usually have a good prognosis. On the other hand, the outlook, with isolated lesions on the ventricular bands, is not so good, as occasionally they develop rapidly and become complicated with oedema and ulceration. One site of a tuberculous lesion must be mentioned because of the extreme hopelessness of the prognosis. If the infiltration invades any part of the soft palate or fauces, no matter how slight the area of laryngeal infiltration may be, no response will be obtained from treatment. I do not think any such case has been known to recover, and unfortunately the patient usually suffers from a most distressing and persistent dysphagia.

GENERAL ASPECTS

There are few conditions in which temperament plays a more important part in determining a patient's future than in tuberculosis, and I think the complication of

laryngitis is considerably influenced by the patient's nature and attitude towards life. As you know, the treatment is exacting and tedious, involving a considerable amount of sacrifice of comfort and pleasure. The undisciplined individual can destroy a fair or good prognosis by inattention to detail and disregard of advice. Similarly, the despondent, morose character will often become progressively worse, although he is most careful to follow out treatment. The latter type is met less frequently than the former, and it is often the irresponsible, careless temperament that ruins the chances of recovery by continual foolish behaviour. The patient must have great moral strength and fortitude to overcome his disability, and the utmost encouragement must be given to him throughout treatment.

I think that the absence of this will power to recover is partially the reason why alcoholics with tuberculous laryngitis have such a bad prognosis. Usually this type of patient suffers from the fibroid type of disease of the lungs, complicated by chronic bronchitis, and has a fair resistance to the infection, but the lack of self control, unrestricted use of the voice (accompanied by excessive smoking), which is so common with these patients, causes irritation which leads to intense congestion of the larynx and a general oedema of the mucous membrane. Contrary to tradition, I find that women keep silence better than men, and are generally much more concerned about the tone of the voice.

It is always interesting to hear the various opinions on the effect of smoking, and the harm or otherwise of a particular type of smoking. Some emphatically deny that the habit in moderation has any influence on the course of the disease, others perceive considerable irritation from the mildest indulgence. Some allow pipes and forbid cigarettes, and some give the reverse advice. Continuous smoking for several years often produces chronic laryngitis, particularly in the cigarette inhaler. This irritation of the mucous surfaces is accompanied by anorexia and chronic intestinal catarrh, with symptoms of increased salivation, followed by dryness of the mouth the next day. It is more the occurrence of these general effects of smoking that hinders the progress of laryngitis in the tuberculous patient than the actual local effect of chronic congestion of the larynx. The average tuberculous patient is a fairly heavy cigarette smoker. If laryngitis develops I think this habit influences the prognosis in proportion to the amount of smoke inhaled. There seems to be no evidence that pipe smoking or moderate cigarette smoking without inhalation has any effect on the prognosis of a tuberculous laryngitis.

EFFECT OF CONCURRENT DISEASE

The prognosis of tuberculous laryngitis is closely connected with the treatment of the pulmonary condition. Those laryngeal cases in which artificial pneumothorax treatment is possible generally show marked improvement of the larynx after the pneumothorax has been established. I find that our own results at Colindale agree with the conclusions of Sir StClair Thomson and Dr. Trail⁶—namely, that an improvement in the laryngeal condition can be expected if the case responds to artificial pneumothorax treatment. Other forms of general treatment, such as sanocrysin and auto-inoculation, do not seem to produce such an immediate improvement in the local condition. The response to treatment brings me to the proposition that the laryngeal condition always follows the progress of the pulmonary lesion. This is not true, otherwise we could not find healed laryngeal infiltration in patients dying from pulmonary disease. Sir StClair Thomson¹ has shown conclusively that occasionally the larynx may improve whilst the lung condition

deteriorates, but the lung condition never improves if the larynx becomes worse. Therefore the onset of tuberculous laryngitis whilst the patient is under institutional treatment means that the patient is going downhill, and is of grave significance. These cases very rarely recover. It will be seen that we have in tuberculous laryngitis an important index of the patient's condition, which if closely observed will give useful information of his or her progress. I agree that the condition of the larynx usually follows that of the lungs, but there is no doubt that in certain cases suitable treatment appears to enable the larynx to heal whilst the lungs are still active, and then, if the lungs relapse, the larynx need not take part in the retrograde movement.

The presence of concurrent diseases will influence the prognosis according to their general effect on the body. Diabetes and syphilis must warn us against being optimistic, although the appearance of the larynx may warrant a good prognosis. On the other hand, the presence of bronchitis, asthma, and pulmonary fibrosis will help us to take a more hopeful outlook. The appearance of the larynx in these cases is apt to be misleading, but it is important to determine the exact amount of infiltration and ulceration present. Often the whole mucous membrane is deeply congested, and may be slightly oedematous. This condition remains stationary for many months, and has little or no significance, being merely a chronic catarrhal condition aggravated by coughing. Debilitating diseases often produce the pale, anaemic larynx, with localized ulceration, which has an unfavourable outlook. Pyorrhoea and stomatitis may cause acute symptoms, but they rarely have any effect on the laryngeal lesion. The occupation of the patient will affect the prognosis adversely if it involves much talking or shouting, or if it leads to the inhalation of irritating fumes and dusts. Pregnancy has a very serious effect on tuberculous laryngitis, particularly if it develops in the early months.

I have been impressed by the improvement of the larynx when nasal and nasopharyngeal obstructions, such as adenoids and deflected nasal septa, have been removed, also when chronic rhinitis has been treated successfully. The removal of such conditions of the upper respiratory tract will improve the prognosis of the larynx.

CONCLUSION

I need hardly stress the influence of early diagnosis on the prognosis. Naturally, the small area of infiltration is more amenable to treatment than the large one, although it must be remembered that the small laryngeal lesion in a patient with little or no resistance will progress rapidly, particularly if the lesion has developed whilst the patient is under sanatorium treatment. Evidence of this low resistance can be obtained by serial blood sedimentation tests, if possible supplemented by cell counts. Finally, I wish to emphasize the necessity of considering the patient's general condition, particularly with regard to his reaction to the disease as shown by the blood picture. This, combined with observations on the site and type of the lesion, will enable us to give a fairly accurate prognosis. The statement that appeared in the *Lancet* in 1922 that "it is universally admitted that tuberculosis of the larynx is a comparatively benign disease which is nearly automatically arrested when the original pulmonary disease becomes quiescent" is too dogmatic and optimistic to apply to such a serious complication; nevertheless, by early diagnosis and correct treatment, we can free ourselves from the dismal prospects of early writers, and confidently feel that in an increasing number of cases the prognosis of the lesion can be moderately, and sometimes very, good.

TABLE I.—Showing the Result of Treatment in the Various Types of Laryngeal Lesions

Type	Clinically Cured	Improved	Stationary	Worse
Extrinsic	1	7	10	13
Intrinsic	6	11	11	6
Localized	8	20	12	2
Lupoid	1	1	1	0

TABLE II.—Showing the Type of Laryngeal Lesion Compared with the Pulmonary Lesion

Type of Lung Lesion	Extrinsic	Intrinsic	Localized	Lupoid
Caseo-fibrotic... ..	20	14	10	0
Fibro-caseous... ..	7	10	16	2
Fibrotic... ..	4	10	16	1

TABLE III.—Showing the Response of the Laryngeal Lesion to Treatment compared with the Type of Pulmonary Lesion

Type of Lung Lesion	Clinically Cured	Improved	Stationary	Worse
Caseo-fibrotic... ..	2	11	17	14
Fibro-caseous... ..	7	15	7	5
Fibrotic... ..	7	13	9	2

TABLE IV.—Showing the Incidence of the Different Types of Laryngeal Lesion at Various Ages

Age	Extrinsic	Intrinsic	Localized	Lupoid
15-20 years	2	4	2	0
20-30 years	4	11	15	1
30-40 years	12	6	7	2
40-50 years	5	7	15	0
50-60 years	5	6	3	0
Over 60 years... ..	3	0	0	0

TABLE V.—Showing the Response of Larynx to Treatment at Various Ages

Age	Clinically Cured	Improved	Stationary	Worse
15-20 years	1	2	2	3
20-30 years	2	12	10	7
30-40 years	3	12	8	4
40-50 years	9	8	7	3
50-60 years	1	4	6	3
Over 60 years	0	1	1	1

TABLE VI.—Showing the Influence of Dysphagia on the Result of Treatment

	Cured	Improved	Stationary	Worse
Suffering from dysphagia ...	3	6	5	13
Not suffering from dysphagia...	19	37	21	6

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THE DURATION OF PASSIVE IMMUNITY TO DIPHTHERIA

BY

E. G. MUNRO JONES, M.R.C.S., L.R.C.P.

LATE HOUSE-PHYSICIAN, NORTH-WESTERN HOSPITAL

AND

JOHN D. KERSHAW, M.B., B.S., D.P.H.

ASSISTANT MEDICAL OFFICER OF HEALTH, EALING

Probably owing to the development of methods of producing active immunity to diphtheria, little investigation has been carried out in recent years on the question of passive immunity. While there is no gainsaying the fact that active immunity is preferable to passive, there is no doubt that, in certain circumstances, passive immunization, when its virtues and limitations are accurately known, may be of considerable value. Apart from its tendency to produce serum sensitivity, the chief disadvantage of passive immunity is its short duration. Investigation of the results obtained and of the opinions held by previous workers showed that, while all were agreed that this immunity only lasted for a short time, the actual duration had been variously estimated by them at from two weeks to two months. It was with the object of obtaining further information on this point that the present investigation was undertaken.

PREVIOUS INVESTIGATIONS

The literature of diphtheria contains little record of previous work on the question, and only three experiments can be traced which bear resemblance to the present study. Kolmer and Moshage¹ investigated the duration of passive immunity to diphtheria as measured by the Schick test. They tested 108 children, aged from 2 months to 3 years, all of whom had received 1,250 units of antitoxin subcutaneously at periods of from one to five days before the test. It appeared that all the twenty-eight tested between five and ten days were Schick-negative, five out of twelve at ten to twenty days, ten out of fourteen at twenty to thirty days, twenty-three out of thirty-six at thirty to fifty days, and nine out of sixteen at over seven weeks.

Apart from the smallness of the numbers in some of these groups, there are two points to which criticism may be directed. First, one expects most children under 6 months to be immune to diphtheria, and such children appear to be included in those under investigation, without any statement as to the proportion they formed of the total. Secondly, no attempt seems to have been made to determine the Schick reaction of the subjects who received antitoxin. It follows that a number of the children injected were, in all probability, already immune; the results, therefore, will tend to exaggerate the duration of immunity. A second investigation carried out by Kolmer and Moshage on 362 scarlet fever patients is subject to criticism on the same grounds. These patients received 2,500 units of antitoxin; 10 per cent. were Schick-positive after one to ten days, 13.9 per cent. after ten to twenty days, 22 per cent. after twenty to thirty days, 34 per cent. in thirty to forty days, 66.7 per cent. after forty to fifty days, and 67.8 per cent. after fifty days.

Zuckerman² carried out a preliminary Schick test, and also repeated his antitoxin dose after the return of the Schick-positive condition. All his patients were tested on alternate days until they gave a positive reaction. Of his twenty-seven cases nineteen received 1,000 units of