It may be a neuritis involving any nerve. The tender toe of typhoid convalescence is of this nature. Meningitis is not a frequent complication, though a large number of patients do suffer more or less cerebral irritation; a few cases of brain abscess have been reported. Hoffman has described an atrophy of the brain, with a widening of the ventricles. Degeneration of the ganglion cells has been demonstrated.

In the eye necrosis of the cornea, thrombosis of the ophthalmic and orbital veins, emboli of the arteria centralis retinae, or optic neuritis with atrophy of the disk may occur.

CONCLUSION. It is possible to have a complication or sequel of typhoid fever at any time during or after the course of the illness, and in any structure of the body where the bacillus may venture or its toxin permeate.

THE LARYNGEAL COMPLICATIONS OF TYPHOID FEVER.

WITH THE REPORT OF TWO CASES.

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LARYNGEAL inflammation as a complication of typhoid fever was first observed and reported by Bayle.¹ A medical student convalescent from abdominal typhus, developed hoarseness, followed by œdema glottidis; an attempted tracheotomy was unsuccessful, the patient succumbing. Bayle's second case, also, was in a male adult who died of suffocation while convalescent on the twenty-ninth day of the disease, without any effort at operative interference. Isolated cases were reported from then on in the French literature, and in 1818 Joseph Frank of Leipzig, reported 2 cases based on the postmortem findings of Pommers and Horn. In 1825 Bouilard reported a case observed by him in 1822. A student of divinity, discharged from the hospital as cured, was admitted for hoarseness, cough, and dyspnoea. He died three days later without operative interference. The despair of these hapless sufferers has been faithfully portrayed by the early writers. Most of these tragic deaths occurred during convalescence or after the patient had been discharged as cured.

Louis, in his classical publication on gastro-intestinal diseases and abdominal typhus, in 1829 reported 4 original cases with necropsy findings. In the same year, Poekel, a military surgeon in the Braunschweiger Militär-Lazareth, performed the second authentic tracheotomy in typhoid laryngitis. The patient, a young man, convalescent of the fever, developed acute perichondritis with œdema glottidis.

¹ Société de médecine de Paris, August, 1808.

The operation gave immediate relief with ultimate recovery. This was the first successful tracheotomy in typhoid affections of the larynx. This patient breathing through his cannula, but otherwise hale and well, was still under observation in 1869.

The use of laryngeal bougies and efforts at dilating post-typhoid laryngeal stenosis were first attempted by Deschange, of Paris, in 1848. The results appear not to have been favorable, since in no case was laryngeal function regained, although an improvement in phonation was observed. Porter² reported 2 cases tracheotomized, with recovery; the first recorded in England.

W. W. Keen,³ of Philadelphia, in 1876, summarized the entire literature pertaining to this condition, collecting 169 cases. These he classified clinically and pathologically, giving to the profession a lucid and instructive description, the most complete in its consideration of the subject that had appeared up to that time.

In 1884, A. Luning,⁴ of Zürich, in an exhaustive thesis⁵ again collated the literature, collecting 192 cases to which he added 2 of his own and 12 others with clinical data. From Luning's description it is evident he had no knowledge of Keen's earlier monograph, most of his collected material being presumably identical with that of Keen, who so assumes in his volume on *The Surgical Complications and Sequelæ of Typhoid*, published in 1896, wherein he completes his earlier work by adding Luning's 14 original cases and such others as had been reported since, his total being 221 cases.

In 1903, Homer Dupuy,⁶ of New Orleans, reported 1 case with 34 collected ones; and, in 1905, Chevalier Jackson⁷ published the collective findings of a routine laryngoscopic examination of 360 typhoid-fever patients in the Western Pennsylvania Hospital.

By a careful search of the accessible literature, I have collected 23 cases—reported since the publication of Dupuy's paper—by Francillon,⁸ Halbrook,⁹ Picot,¹⁰ Johnstone,¹¹ Quinlan,¹² Boston,¹³ Del Aqua,¹⁴ Day and Jackson,¹⁵ Chevalier Jackson,¹⁶ Roque et Basset,¹⁷ Herbert,¹⁸ Pater,¹⁹ Wilson,²⁰ Pierat and Stordeur,²¹ Weil and Lemaire.²² These, with my own two cases, bring the total to

² Dublin Med. Journal, 1836.

³ Keen's Toner Lecture.

⁴ Deut. Archiv f. klinische Chirurgie., 1884, Band. xxx.

⁵ Über die Laryngo- und Tracheo-Stenose und ihre chirurgische Behandlung.

⁶ New Orleans Medical and Surgical Journal, 1903.

⁷ Amer. Jour. Men. Sci., 1905.

⁸ Bull. et mém. hôp. de Paris, 1903, p. 257.

⁹ Bull. et mém. de Soc. anat. de Paris, 1903, p. 699.

¹⁰ Gaz. hebdom. de sci. med., Bordeaux, 1904, p. 98.

¹¹ New York Med. News, 1905, p. 1021.

¹² Laryngoscope, St. Louis, 1905, p. 17.

¹³ New York Med. Jour., 1907, p. 301.

¹⁴ Clin. et prat. Treviglio, 1905, p. 146.

¹⁵ Annals of Otology, Rhinology, and Laryngology, 1904, p. 24.

¹⁶ Amer. Jour. Men. Sci., 1905, p. 861.

¹⁷ Lyon médicale, 1903, p. 269.

¹⁸ Chicago Medical Recorder, 1904, p. 509.

¹⁹ Bull. et mém. Soc. anat. de Paris, 1904, p. 38.

²⁰ Jour. of Michigan med. Soc., Detroit, 1904, p. 400.

²¹ Jour. med. de Bruxelles, 1907, p. 82.

²² Archiv. intern. de laryngol., Paris, 1906, p. 899.

281, which, omitting Jackson's studies, include practically all the cases heretofore reported.

ETIOLOGY. As causative factors are to be considered:

1. The friction and irritation of the physiological acts of phonation and swallowing, and the pathological act of coughing, trifling insults in themselves, but constant in their repetition—operating on a surface which is part of an organism suffering from a general typhoid toxemia.

2. A mucous membrane itself in a state of catarrhal inflammation with swollen surface epithelium.

3. Thermic influences, such as heat or cold, or both in rapid succession, including sudden drafts.

4. Bacteria. That lymphoid tissue, regardless of its distribution in the human economy, may be subject to primary invasion by the Eberth bacillus is now accepted by most observers. The bacilli have been isolated in sections, and grown in pure culture from the larynx by Schulz²³ in 1894, W. Williams in 1901,²⁴ and R. W. Weil²⁵ in 1905. Herbert and Liebman²⁶ and also Chevalier Jackson²⁷ cultivated it in pure growth from the pus of perichondrial abscesses. The Klebs-Loeffler bacillus has been isolated in pure culture and as a mixed infection, the earlier pathologists recognizing a membranous or diphtheritic and a simple ulceration in typhoid fever. The streptococcus and other pathological bacteria usually present as a secondary infection may act as the primary factor. Roberts²⁸ reported a case of Ludwig's angina complicating typhoid fever, in which he succeeded in demonstrating streptococci in pure form. Murray²⁹ in 1903 reported a similar case.

5. In my own Case I, the submucous infiltration of the aryteno-epiglottic folds was due to a direct extension of the pharyngeal involvement in a double parotitis.

6. Ditricks attributed to dorsal decubitus a role in the etiology, holding that by gravity a venous stasis with softening of the tissues of the posterior laryngeal wall might be produced, inviting abrasion and injury; and in the light of our present knowledge of the physical processes on immunity,³⁰ it is not unlikely that the decubitus weakens the native resistance of the mucous membrane to the entry of pathogenic organism.

PATHOLOGY. Ulcerative lesions of the larynx in typhoid fever, while recognized by the early pathologists, were considered an accidental foreign infection, Rokitsansky of Vienna, in 1842, being the first to give this lesion careful study. With wonderful intelligence he anticipated our present conception of it, referring to it as a true

²³ Berl. klin. Wochenblätter, Band, xxxv.

²⁴ Trans. New York Path. Soc., 1905.

²⁵ Ibid.

²⁶ American Medicine, 1903.

²⁷ Jonathan Wright. New York Med. Journal, 1907.

²⁸ Diseases of the Upper Respir. Tract, 1901.

²⁹ Chicago Med. Recorder, 1905.

³⁰ American Medicine, 1901.

metastasis of the typhoid poison, in every sense analogous to the developments in the intestinal mucosa. Keen, in 1876, classified the lesions according to the degree or depth of tissue involvement, as inflammatory or submucous laryngitis, ulcerative laryngitis, and laryngeal perichondritis, of which neither stage can be sharply outlined, they at times overlapping one another. The frequency of its occurrence is stated by Luning to be 12 per cent., basing his statistics on 1032 autopsies. Of the 2000 Munich cases 10.7 per cent. showed laryngeal ulcer, and J. C. Baer²¹ found laryngeal ulcer in 3.4 per cent. of 89 autopsies held at the Presbyterian and the Cook County Hospitals of Chicago.

The type of lesion most prevalent varies with the material of the observer. Luning divides the 12 per cent. of laryngeal lesions into 1.5 per cent. of simple or submucous laryngitis and a little over 5 per cent. each of ulcerative laryngitis and laryngeal perichondritis.

DISTRIBUTION. The findings at autopsy do not accord with clinical observation. In over 4000 autopsies collected by Luning, and his agree with the observations of Keen, the posterior laryngeal wall at the insertion of the vocal chords involving the cricoid cartilage, was the seat of the lesion in 60 per cent. The arytenoid cartilages and interspace the next, the aryteno-epiglottidean folds, epiglottis, and thyroid cartilage being least affected in the order named. Chevalier Jackson, in his series of 360 routine laryngoscopic examinations in typhoid fever subjects found ulcer present in 68 cases; the frequency of distribution being: epiglottis 42 times, aryteno-epiglottidean folds 22, interarytenoid space 18, and arytenoid cartilage 10.

Laryngeal inflammation may occur at any time between the first and the tenth weeks. Over 70 per cent. of the cases reported occurred after the third week. Of mine one was in the third and one in the sixth week. Ulceration of the larynx, shown by the collective statistics of all observers to be present in typhoid fever in from 10 to 18 per cent. of all the cases, is clinically diagnosed in only a very small percentage of this number, perhaps one in twenty or less.

Clinically, the onset is, as a rule, insidious and unobserved. If it be during or before the fastigium, the patient, with sensibility benumbed, is too apathetic and indifferent to pain to make complaint, or delirium may becloud the symptoms. Extreme dyspnoea and suffocative spasm may be the first intimation that even a close observer may obtain of the grave process transpiring. In this asthenic state, the first attack may terminate fatally, or with great and agonizing effort the patient will cough up blood, stained sputum and serum, with temporary relief and easier breathing, only to be followed by recurrent seizures. In the greater number, however, this complication occurs when convalescence is well established; doctor and patient both secure in the belief that all danger is past

²¹ AMER. JOUR. MED. SCI., 1905.

and no further difficulty need be anticipated. And equally to be dreaded here, is the stealthy onset masked by the treacherous mildness of the symptoms. These are in the order of their frequency: hoarseness, voice change, aphonia, inspiratory stridor, dyspnoea, cough of metallic or laryngeal character, and dysphagia. Any of these may be overlooked or misconstrued by the attendant as a manifestation of a simple post-typhoid asthenia, until, with tragic unexpectedness, an acute oedema of the glottis involves the sufferer in a desperate struggle with death. Or, again, without any of the violent respiratory exertion usually preceding suffocation, an asthenic apnoea, may, without the slightest warning of its approach, terminate life. Indeed, so sudden, terrible, and menacing to life are these conditions that they demand immediate and the boldest action. Surely foolhardiness has no place in the practice of medicine, but in a developing oedema glottidis, or threatened apnoea, timidity may be even more destructive to life, and prompt operative relief is the rational and conservative indication.

My Case II and one reported by J. W. Boyce²² are cited in illustration:

J. H., admitted to Dr. Zemansky's service in convalescence from typhoid fever, on the tenth day in the Hospital and the thirty-seventh day since the onset of the fever, developed some hoarseness and a higher pitch of voice, with metallic cough, and inspiratory stridor. There was no dyspnoea or dysphagia. Laryngoscopy showed slight congestion of the laryngeal mucosa, with no ulceration or restricted movements of the cords. The symptoms were not at any time considered urgent, and with cocaine locally (2 per cent. spray) and ice externally, appeared speedily to clear up, so that no further trouble was apprehended; when without any further warning, forty-eight hours after the first signs, the patient developed an acute oedema of the glottis, with suffocative spasm, causing cyanosis and unconsciousness. An immediate laryngotomy performed with an ordinary pocket penknife, by Dr. London, of the house staff, saved the patient's life. So acute was the emergency that there was no time to send for instruments.

Boyce, of Pittsburg, reports a patient with laryngeal complication, who was taken to the operating-room to be tracheotomized as a precautionary measure, not because it was needed, but for fear it might come to be during the night in the doctor's absence. During the leisurely preparations for a systematic operation, he accidentally noticed that the patient had stopped breathing. The surgeon standing by with knife in hand was able to stab the patient on the instant, and it required ten minutes of artificial respiration before the patient could be trusted to do his own breathing. Dr. Boyce states there would have been no time to send to another room for instruments.

²² *Annals Otology, Laryngology, and Rhinology.*

May such conditions not account for some of the unexplained, sudden deaths occurring during typhoid fever? It were far better, if by clinical signs and laryngoscopy, an early diagnosis were made and such emergency work anticipated by early and timely operation, with due surgical precaution.

In typhoid fever the slightest hoarseness or change of voice or cough should at once awaken suspicion, and in every case laryngoscopic investigation should be instituted; no complaint of pain, however slight referred to the throat in breathing or in swallowing, should fall on deaf ears; for in the words of W. W. Keen, such complaints may be "the vagaries of a delirious mind, but they may also prove to be the heralds of the greatest danger."

PROGNOSIS. Appended below are tables giving the general result of 243 collected cases of which clinical data were obtainable. The columns represent: (1) The entire mortality percentage, (2) the mortality percentage of operated cases, and (3) the mortality percentage of non-operated cases.

Collected by	Died.	Recovered.	Operated on.		Unoperated on.	
			Died.	Recovered.	Died.	Recovered.
W. W. Keen . . . 197	132	65	55	44	77	21
Homer Dupuy . 26	13	13	7	6	9	4
Rieser 20	13	7	13	4	1	2
Total 243	158 or 65 %	85	75 or 58 %	54	87 or 76 %	27

These statistics would show laryngeal inflammation in typhoid fever to be a complication with a death rate next to that of intestinal perforation. They are not conclusive, however, since it cannot be stated how many of these fatalities are directly chargeable to the laryngeal condition and how many to the underlying general infection.

The comparison of the tables of mortality of the operative with the non-operative cases forms a convincing argument for operation; and it may be said that careful laryngoscopic observation with early operation will very greatly reduce an appalling, and, in part, a preventable mortality.

Of Jackson's 68 cases, 8 were tracheotomized, and not one death in the 8 was directly referable to the laryngeal complication.

TREATMENT. The first impulse after having made a diagnosis of laryngeal inflammation in typhoid fever should be to place the patient in a zone of safety—by that I mean under constant and competent observation—in readiness for immediate operative relief should demand therefor arise. Having thus secured the patient, steaming the larynx, or ice by the mouth, or an external pack may be

tried. Spraying locally with a 2 per cent. solution of cocaine or a 1 to 1000 solution of adrenalin chloride at times gives relief, blanching and contracting the tissues if the inflammation be slight and transitory; such medication may tide the patient over. If, however, symptoms be persistent or become aggravated, or if stenosis be established restricting the laryngeal function, operation should be resorted to, laryngotracheotomy being the rational measure. Intubation with the O'Dwyer tube has been performed with success, but is not an advisable operative proceeding; of 5 cases^{33 34} reported within the last two years in which intubation was performed, the results were unsatisfactory and later tracheotomy had to be resorted to in each case. By use of the tube in abscess formation or sloughing perichondritis, free drainage is interfered with. The danger of plugging is great and constant, and in the vitiated condition of the laryngeal tissues, the pressure of the tube itself may add to the existing ulceration.

The treatment of post-typhoid stenosis of the larynx and trachea belong to the domain of laryngology and it is not the purpose of this paper to discuss it.

CONCLUSION. Pathological involvement of the larynx is very much more frequent than is clinically diagnosed. Clinically, laryngeal involvement may constitute one of the gravest complications of typhoid fever; the stealthy and sudden onset of œdema makes it particularly to be dreaded. Early tracheotomy is the rational and life-saving operation and should be performed as soon as stenosis is positively established. The frequency of this complication pathologically, and the possibility of its extreme clinical gravity, warrant that it receive more careful consideration than it has heretofore received in the text-books, in discussions of typhoid fever, and at the bedside of the patient.

CASE I.—*Typhoid fever; intestinal hemorrhage; double parotitis with unilateral suppuration and œdema of the glottis.*

L. R., aged seventeen years, white. Born in United States. Occupation, optician's apprentice. Admitted to the service of Dr. A. P. Zemansky April 11, 1907.

The patient, a fully developed adult male, of large frame, had been in care of his family physician and came to the hospital in the second week of his illness, which had been diagnosed as typhoid fever. From the time of his admission to April 21, the disease seemed to run a mildly even course. The temperature fluctuated between 102° and 103.4°; pulse from 80 to 90. Rose spots were present, and the spleen was enlarged. Leukocyte count 8600, with 32 per cent. lymphocytes. Widal reaction positive.

On April 22 and 23 the patient had recurrent, large intestinal

³³ J. H. Quinlan. *The Laryngoscope*, St. Louis, 1905.

³⁴ W. L. Boston. *New York Med. Journal*, 1907.

hemorrhages, with wide fluctuations in the temperature curve and presented the clinical picture of a severe and increasing toxemia.

April 24. Patient in a state of muttering, restless stupor. Tongue dry. Slight swelling observed beneath the left ear involving the parotid gland.

April 25. General condition unchanged, left parotid gland and entire cheek swollen, red, shining, and very tender. Right parotid gland slightly swollen. Blood examination: hemoglobin 70 per cent.; white blood count 8600.

April 27. Face very much swollen; deglutition difficult and painful. The pharyngeal tissues are deeply injected and swollen, almost occluding the pharyngeal cavity. Attempted laryngoscopic examination difficult and unsatisfactory. Temperature, 105°; pulse, 120; respiration, 30. Patient in stupor and very restless.

About 3 P.M. respiration became labored and difficult; lividity and cyanosis gradually developed, clearly indicating that the supraglottic laryngeal tissues had become involved and edematous.

A high tracheotomy was performed with immediate respiratory relief. The patient remained in a stuporous condition thoroughly overcome with the severe typhoid toxemia, and died without regaining consciousness on April 28, at 12.25 P.M.

Cultures for Klebs-Loeffler bacillus from smears by the mouth and through the cannula were negative.

At postmortem, wound examination, to which we were restricted, showed the cartilaginous box of the larynx and the trachea absolutely normal. Firm pressure over the left parotid gland caused a free flow of pus through the left auditory canal.

CASE II.—*Typhoid fever with submucous laryngitis and acute edema of the glottis.*

L. R., aged twenty-four years, white. Born in Germany. Single. Occupation, shipping clerk. Admitted to Dr. A. P. Zemansky's service April 12, 1907.

Patient, a well-built adult male, was admitted convalescent, in the fourth week of typhoid fever. The clinical course had been mild and without complication—his chief complaint now being marked asthenia.

From the time of admission to April 20, the patient's temperature was normal, and a gradual, steady improvement in his general condition was observed. Widal reaction positive.

On April 20 he developed hoarseness with slight cough, and an inspiratory stridor which seemed at times to become harsher, and then again entirely to disappear. There was no dyspnea or dysphagia, and no complaint of other discomfort. Laryngoscopy showed some injection of the vocal cords without ulceration, or apparent restriction in movements.

Ice externally and by the mouth with a local spray of 2 per cent. solution of cocaine hydrochloride was ordered, the patient being kept under close observation.

Repeated laryngoscopy on April 21 showed no further lesion. The symptoms had apparently cleared up under treatment, there remaining only a persistent aphonia.

April 22. At 9 A.M., after a good night's rest, the patient very suddenly developed respiratory obstruction, became deeply cyanosed and was threatened with immediate suffocation. So sudden and complete was the development of this stenosis as to demand instant operative relief.

Laryngotomy by incision through the cricothyroid membrane was performed, and tube inserted by Dr. London of the house staff, who used an ordinary pocket penknife, the condition being too urgent to risk the delay involved in sending to the operating-room for instruments. Relief was prompt, cyanosis at once disappearing; respiration through the cannula became regular and unobstructed.

Swabs taken by the mouth and the cannula for cultures of Klebs-Loeffler bacillus proved negative.

June 1, 1907. The patient is still under observation and wearing the cannula. Laryngoscopy shows marked injection of the cords at their posterior commissure with restriction of movement. There is no visible ulceration. An attempt to remove the cannula was made about ten days after operation and once since then, but laryngeal breathing becoming difficult after three or four minutes, made it necessary each time to replace the cannula. Excepting a slight febrile reaction the temperature rising to 101.8° on the second day after operation, the patient's general health has not suffered any from his laryngeal complication.

PURULENT CEREBROSPINAL MENINGITIS CAUSED BY THE TYPHOID BACILLUS, WITHOUT THE USUAL INTESTI- NAL LESIONS OF TYPHOID FEVER.

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WILLIAM W., colored, aged thirty-four years, a native of Virginia, a coal picker by occupation, was admitted to the Philadelphia General Hospital, to the service of Dr. F. P. Henry, on account of headache, dizziness, constipation, and fever. His father and mother are dead; cause unknown. His wife and one child are living and well.