LVIII.

CAVERNOUS SINUS THROMBOSIS DUE TO ORGANISMS OF THE STREPTOTHRIX GROUP.

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Since 1907, when Löhlein reported his case of brain abscess resulting from a streptothrix infection, nothing of importance has appeared in the literature concerning this phase of the disease.

It is my good fortune to be able to add a little to the knowledge of this interesting subject and to report a case which seems to be absolutely unique in the scattered literature of the streptothrix infections.

Although there are numerous records of cases where the cause of death was proved to be an infection from streptothrix in various parts of the body, the cases combined with intracranial complications are comparatively rare, and, what interests us from the standpoint of otologists, intracranial complications originating from ear infections seem to be absolutely unknown.

In this article our interest has naturally been centered only on those cases in which the brain and its meninges have been involved.

The first case of this nature to be fully described and worked out bacteriologically was reported by Eppinger in 1890.⁶⁷ He was able to cultivate a mould from a metastatic abscess in the brain, and named the organism *cladothrix asteroides*, but this has since been identified as a true streptothrix and is now called streptothrix Eppengeri. He found this organism pathogenic for rabbits and guinea pigs, and was also the first to see the very great resemblance to tubercular processes and therefore designated the disease as pseudotuberculosis cladothricia, a

similarity which Flexner studied later and agreed to. In fact it is through this research that the recent work on the true botanical place of the tubercle bacillus was started.

In the same year Armquist also isolated a streptothrix from a meningeal exudate which occurred in connection with other mycelial forms.

Various fatal cases of streptothrix infections were now reported. Tschierschke (1891), Hesse (1892), Carten, Gruber (1893), and finally Riviere and Sabarez, in 1894, reported two cases, one of which again showed a metastatic brain abscess originating in a probable lung abscess. The streptothrix was isolated from both abscesses. In the same year Ferre and Faquet also isolated the organism from a brain abscess. Many interesting cases, not of intracranial origin, were reported by various authors, and again, in 1899, Ferrari described a metastatic brain abscess of this character, probably originating in broken down bronchial glands.

The next case which interests us was that of Chiari, who reported two cases of bronchiectasia which were complicated with meningitis. In 1903 both Horst and Löhlein reported a case in which multiple abscesses due to a streptothrix infection were found at autopsy, and again, in 1907, Löhlein had the good fortune to be able to report still another case of brain abscess of the same origin. From this time up to the present writing there seems to have been no other cases reported, and it can, therefore, be seen that the number of cases of brain complications following streptothrix infections is extremely small, probably not over ten all told; and as far as a careful review of the literature shows, none at all that started in the middle ear and later led to an involvement of the great blood sinuses of the brain.

The morphologic position of the streptothrix group is to some extent an unsettled problem, but it seems as if we ought to be willing to accept the carefully worked out life history, as given by Foulerton, who does not consider that the group should be classed as bacteria but as moulds.

If we look over the literature of the ear moulds, we find that the majority of the cases reported have usually been classed under the heading of mycosis, aspergillus or allied forms. These are clinically and morphologically unrelated to the streptothrix group, and as far as is known have never led to

intracranial complications. They are generally confined to the external auditory canal, but in a case reported by Haug, he described the mould as extending into the cells of the mastoid process, and only a few cases of middle ear infection have been traced to this source.

Like many other botanical groups, the nomenclature in the earlier works on this subject has been very loosely applied, and, therefore, there is considerable confusion as to whether the streptothrix is related to the actinimycoses. This, however, is not the case, for in the life history of the streptothrix there are such marked differences that their identity with the latter group is at once excluded.

As nearly as can be determined, the name streptothrix was first utilized by Corda in 1834, but the identify of his organism is somewhat in doubt. Probably the mould isolated by Cohn (1874) from the lacrimal canal is the same as we today recognize under the title of streptothrix. The further historical development of the subject has been worked out in Foulerton's article and need not be repeated here.

Inasmuch as it is the opinion of the author that this organism is far more common in otologic infections than has generally been reported, a short description of the morphologic characteristics will not be out of place. The description is borrowed freely from Foulerton's article and is here added, as it would seem practical to have the first article dealing with the subject from the otologic standpoint as complete as possible, and thereby obviate the necessity of reference to the original sources.

Starting from the original spherical spore, growing in artificial media, under suitable conditions of warmth and moisture, two or three small buds project and, gradually elongating, become the primary filaments of the mycelial mass. From the primary filaments lateral branches bud out, and from these secondary branches other lateral filaments again grow out by a repetition of the budding process, and in this manner a more or less dense and tangled tuft of wavy branching mycelium is formed.

The termination of the filaments presents various appearances in different species, and the appearance may not be constant in the same species; the end of the filaments may be pointed or rounded off, or may present small spherical or Indian-

club shaped enlargements. The adult mycelium presents a homogeneous appearance when stained with the ordinary basic anilin dyes or by Gram's method; when segmentation occurs there is an alteration of the staining properties, resulting from a degeneration of shorter or longer segments of the constituent filaments occurring at irregular intervals along their length. The degenerated portions of the filaments no longer retain the stain when treated by Gram's method, and stain but faintly with basic anilin dyes employed in the usual way. Fragmentation of the mycelium follows on segmentation, the degenerated segments gradually disappear, and in the place of the original tuft of branching mycelium there are collections of separate, shorter or longer, lengths of the filaments, which may appear as straight or slightly curved rods, or may retain the wavy outline of the original mycelium, or may present a well-marked corkscrew or spirillum shape.

It is quite certain that the rod segments never give rise directly to new rod segments by a process which is in any way analogous to the fission process which is a characteristic of the bacillary forms of the schizomycetes.

From the above description and from observation it can be stated that the morphology of the streptothrix is widely different at different stages.

In some of the pathogenetic species of streptotricheæ it is impossible to trace the complete morphology on any sort of media, the mycelium develops very slowly, and segmentation and fragmentation of the filaments appear to occur coincidentally with the growth. In such cases the ordinary cover glass preparation will show little more than closely packed masses of rod segments which often have a beaded appearance, the whole closely resembling what is seen in a similar preparation from a culture of bacillus diphtheriæ or bacillus tuberculosis.

With but a few dissenting voices, the place which the genus streptothrix belongs in botanical classification is among the hyphomycetes or mould fungi. The dissenters from this view would regard the branching mycelium, the rod segments, and the spherical spores as merely casual morphologic variations of a highly pleomorphic fission fungus, which under different conditions may assume a branching filamentous, a spirillar, a bacillary, or coccal form.

The streptotricheæ, both the saprophytic and the pathogenetic forms, are very widely distributed in nature. In the higher animals we have the streptothrix bovis communis and streptothrix nocardii, occurring commonly in cattle. Numerous other species have been described, but as yet no carefully worked out case of these species as occurring in man has been found.

One or two fairly dependable cases of streptothrix bovis communis have been reported as occurring in man, but other than these few cases which might point to the lower animals as a source of infection, we are at loss to give a satisfactory explanation of the original source of the infection.

The frequency of primary streptothrix infection of the mouth in cattle, resulting in the formation of small nodules situated immediately under, and sometimes actually invading, the mucous surface of the dorsum of the tongue, has obviously suggested that herbage may be a special habitat of the streptotricheæ and a possible source of infection. Further, the general belief that these infections are especially liable to occur among those whose occupations bring them into frequent contact with dust emanating from dried grass, is to some extent supported by a consideration of the habits and occupation of thirty-nine individuals above mentioned. Thus, there were four men employed in stables, constantly handling hay and straw, and possibly addicted to the habit, prevalent among those employed in stables, of chewing pieces of straw. Two of the patients were gardeners, two cases occurred in bakers, and one patient was a dairy maid.

There are certain new features covering the pathogenetic action of this organism in the case about to be described which make it necessary to refer once more to the general literature and to show what the generally accepted opinion is regarding this point.

The only cases which are at all similar to ours are the ones which refer to intracranial complications. Here the occurrence of the metastatic brain abscess is the predominating type. As seen in other parts of the body, the infection causes the development of nodules and larger masses of granulomatous tissue around the invading parasites. These masses may cicatrize or break down into abscesses.

Speaking generally, it may be said that the streptotricheæ

which are the cause of human infection are not of themselves apt to produce any very marked constitutional symptoms or effects, either by the secretion of actively virulent toxins or by the production of like bodies by decomposition of the tissue in which they may be growing.

The uncomplicated action of the streptotricheæ, then, is not usually manifested by severe general symptoms, but rather in the physical results of the tissues actually infected. Generally it is only when the granulomatous tissue, having broken down, has become the seat of infection, or secondary infection by pyogenic cocci or other organism which secrete toxins having a marked general effect, that the wasting and more severe constitutional symptoms which occur in advanced cases of streptotrichosis are seen.

This general review, then, will serve to introduce the case in hand and serve as a basis for the consideration of some new points which it seems to illustrate.

C. Q., Italian, twenty-five years old. Admitted to the San Francisco Polyclinic and Postgraduate School's service at the San Francisco City and County Hospital, June 15, 1912. Died on same date. The patient was admitted with the general diagnosis of gonorrheal ophthalmia.

Past History.—Sensorium of patient entirely clear, all questions answered by aid of interpreter. Patient has been ill for about forty-five days. At that time he had an attack of right sided earache with a discharge of reddish, foul smelling pus. He gives history of repeated attacks of otorrhea since childhood, with periods of what he considered complete cessation of all symptoms.

About twenty-one days ago he had an attack of vomiting, dizziness, sweating and unsteadiness of gait. He had no chills, but he himself noted stiffness of neck. At this time he was admitted to a local hospital, where he was treated for meningitis with five injections of the original Schafer's serum without any apparent benefit. June 11th, a beginning exophthalmus was noted. The nose was examined for a suspected sinus infection, but unfortunately the ears were not examined. At this time the eye grounds were pronounced normal. The patient was discharged from the hospital the following day because of lack of funds. June 13th, patient had acute

attack of dizziness, nausea, vomiting, severe disturbance of equilibrium, followed by severe chill.

General Examination.—Small, delicately built man, unable to speak English, sensorium absolutely clear. Temperature 102°, pulse 100, full and bounding. Neck absolutely rigid. High grade of double exophthalmus. Incomplete closure of eyelids. Lies flat on back, takes no notice of surroundings, unless spoken to, and continuously moans from pain in head. Locates intense headache behind eyes and over frontal lobes.

Physical Examination.—Chest.—Loud crepitant rales on both sides.

Heart.—Sounds fairly strong, rapid and no murmurs.

Reflexes.—Very slight knee jerk right, absent left. Abdominal reflex absent. Tendon reflex absent. Kernig's sign present, positive and marked. No Babinsky.

Urine.—Slight amount of albumin, otherwise normal.

Blood.—Reds 4,500,000. Whites 45,000. Polymorphonuclear 84 per cent.

Spinal Puncture.—Fluid under great pressure, turbid, many white cells. Repeated stains show no bacteria and no growth on several media.

Examination of Eyes. (Dr. Vard Hulen.)—Marked double exophthalmus, equal on both sides. Eyes divergent. Intense chemosis, especially in lower part of ocular conjunctiva. Extremely well marked swelling between eyes, extending up over the skin of forehead. The skin is hot, red in color and brawny to the touch. There is marked pressure sensitiveness at this point, but nowhere else.

Pupils normal in size and reaction. Vision, O. D., 12/200; O. S., 8/200. Cornea clear except little haziness of both lower margins. Atropin dilates pupils evenly and widely.

Ophthalmoscopic Findings.—Extensive neuroretinitis with marked retinal edema. No signs of choked disc.

Clinical Diagnosis.—Secondary orbital cellulitis. No fluctuation of tissue around eyes. No diagnosis of intracranial complications possible from background findings.

Examination of Ears. (Dr. Henry Horn.)—Left ear normal. Right ear: Very slight tenderness over right mastoid, no swelling or edema. Some tenderness along right jugular. Right submaxillary gland somewhat swollen. External canal filled with whitish debris, small amount of pus, no odor. Ear

washed. Total destruction of drum; middle ear some smaller than usual on account of swollen mucous membrane. Upper part of external canal somewhat sunken. Weber to left. Bone conduction slightly shortened (?). Rinné negative. Hears loud shouts, with Bárány apparatus in other ear. Five minutes' irrigation with cold water produces no nystagmus and no dizziness. No spontaneous nystagmus.

Operation.—Ether narcosis, one hour and thirty minutes. Patient left table in fine shape. Pulse and respiration good. Rapid sinking and death after few hours.

The fact that the eye examination gave the impression that the exophthalmus was not due to an intracranial complication, but due to an orbital cellulitis, and the evident involvement of the sigmoid sinus and right jugular, the fair condition of the patient and the free sensorium, combined with the absolutely fatal prognosis without operative interference, were the indications for operation.

Mastoid Operation.—Usual incision. Soft parts not swollen. Few if any cells in mastoid tip involved. Sinus located far forward and only a few millimeters from the external bony canal. In spite of most careful search no antrum could be found at operation. (Its absence was afterwards confirmed at autopsy.) Middle ear filled with whitish débris, which did not give the impression of cholesteatoma, and on the other hand did not resemble any pus collection which the author had ever seen.

Sinus Operation.—Sinus laid free for an inch or more. The wall of the sigmoid sinus was entirely broken down, the clot had disintegrated and was filled with yellowish débris without odor. The thrombotic process evidently extended into the bulb and the same was rapidly and thoroughly laid free. It was seen that the jugular would have to be explored, so the uncovering of the lateral sinus was first extended about an inch toward the torcular, or until free bleeding occurred, and this was controlled with iodoform gauze tampon. The character of the thrombus changed completely as the torcular was approached, from a septic, markedly purulent mass to a reddish blood clot, which was not broken down. The free bleeding then occurred.

Ligation of the Jugular.—Incision from angle of jaw to clavicle, along the anterior border of the sternomastoid mus-

cle. Large mass of infected glands in upper third of neck had to be dissected free in order to expose jugular. Facial vein ligated, although it was not thrombosed. Ligation as close to clavicle as possible, evidently well beyond thrombus. The entire vein was thrombosed with the same reddish clot as found near torcular, and was removed en bloc. Bulb washed out from above. Upper end of vein sewed to upper angle of skin incision, after the method of Alexander. Wound closed, free drainage from lower angle.

The operative findings proved without doubt that we had to do with a far more extensive sinus involvement than was possible to correct surgically, and as the patient's general condition was good he was sent to ward. Surgical shock showed itself almost immediately, and the patient died in a few hours without recovering consciousness.

The autopsy was made through the courtesy of Prof. Wm. Ophuls, of Stanford University, the findings were dictated to his own clerk, and the subsequent microscopic work was done by him personally. I take this opportunity of expressing my great gratitude for his generosity in allowing me to use the results of his work. There was no indication at the autopsy that we had to do with anything more than an ordinary septic infection, and it was only by the thorough method which all cases are carefully worked out in the pathologic laboratories of Stanford University that the true etiologic factor in this case was discovered.

Necropsy Report.—(Prof. Wm. Ophuls). Strongly built, rather poorly nourished man, of about thirty years of age. There is a very marked exophthalmus so that the lids cannot close. The opening of the lids at present is about 1 cm. The conjunctivæ are extremely hyperemic and edematous. There are large hemorrhages around the cornea. The lids are also congested and edematous. There is marked passive congestion of the lips, of left ear, and of upper part of neck. No palpable enlargement of the superficial lymph glands. No edema. There is a slight yellow discoloration of the conjunctivæ and skin of neck and shoulders.

In back of ear there is a deep wound about 5 cm. in diameter, and extending from that posteriorly, an incision about 6 cm. long. Wound is packed with gauze. The wound extends through the bone to the dura mater, and the dura is exposed

over a large distance. The transverse sinus is opened for a distance of 1 cm., sigmoid sinus exposed to bulb of jugular vein.

On the right side of the neck there is a longitudinal incision reaching from the angle of the jaw down to the sternoclavicular joint on the right side. The wound is drained with cigarette drain. At the bottom of the wound the large vessels are exposed. The jugular vein has been resected practically for the whole distance; the upper end is sutured into the wound. One of the submaxillary lymph glands is moderately enlarged, grayish red and moist.

Skull cap normal. One of the pachionian granulations near the longitudinal fissure extends very far into the bone, the posterior part of the longitudinal sinus has some soft clots and turbid bloody liquid. The dura mater is rather tense on both sides. Pia mater on right side shows marked diffuse hyperemia and some edema. The hyperemia is even more marked of left side. Pia mater at base is also hyperemic and edematous. The right anterior half of the pons shows a very distinct yellowish purulent infiltration; the same posteriorly, about the middle of lower surface of left hemisphere of cerebellum near the median line. On pressure upon cavernous sinus on either side there is a drop of pus discharged at its junction with the petrosus superior. The transverse sinus on both sides is also filled with thick purulent material. Same condition in the sigmoid sinus on the left side.

Soft tissues underneath the roof of the left orbit are full of pus, and there are numerous accumulations of pus underneath in the muscles. Same condition on the right side. Jugular vein on left side of neck is free. Right jugular vein is free below point of resection.

Brain normal, except for hyperemia and edema.

There is a marked atrophy of subcutaneous fatty tissue, the muscles are poorly developed. Stomach and liver in normal position. Transverse colon forms a V-shaped loop and very nearly reaches the symphysis. Few drops of fluid in peritoneal cavity.

Diaphragm.—Fifth rib both sides. Chest is rather poorly arched, long, symmetric. Heart, about three-fourths normal size. Soft postmortem clot in pulmonary artery. The heart valves are normal. Aorta is small. Many small yellow spots

in intima. The bronchi are somewhat hyperemic and contain some mucus. The pulmonary tissue is normal. There is a small superficial scar at the right apex. Right lung same as the left.

Spleen measures one and one-half times normal size. Pulp is soft, of light grayish brown color.

Left adrenal is normal.

Left kidney slightly swollen. Cortex is somewhat opaque.

Right kidney, same as left.

Pancreas, duodenum, stomach, normal.

Liver, tissue hyperemic and moist, somewhat opaque.

The rest of the aorta like the beginning.

Diagnosis.—Purulent otitis media right side (streptothrix infection). Septic thrombosis of sigmoid sinus, of right jugular, of both transverse sinuses, posterior part of longitudinal sinus, both cavernous sinuses. Phlegmon of both orbits. Double exophthalmos. Purulent meningitis. Hypoplasia of heart and aorta. Fatty spots in intima. Parenchymatous degeneration of kidneys and liver. Septic spleen. Terminal icterus. Smears were made from infected sinuses, the meninges and from pus in left orbit. They all show many partly degenerated polymorphonuclear leucocytes, few lymphocytes, many large mononuclear phagocytes. In some of the smears, especially in those from the left orbit, a moderate number of very fine, Gram positive, somewhat irregularly staining filaments with true branching. They are single or matted together in branches, mostly extracellular. No other bacteria found, in spite of intense staining and careful search.

Anatomic Diagnosis.—Purulent otitis media on right side (streptothrix infection). Septic thrombosis of right sigmoid sinus, of the right jugular, of both transverse sinuses, posterior part of longitudinal sinus, left sigmoid sinus, both superior petrosal sinuses, both cavernous sinuses. Phlegmon of both orbits. Double exophthalmus. Purulent meningitis. Hypoplasia of heart, kidneys and liver. Septic spleen. Terminal icterus.

Epikrisis.—This "autopsia in vivo et in mortuo" would seem not only to enable us to add something to the scarce literature of the intracranial involvements following this somewhat rare infection due to the streptotricheæ, but also to draw

a fairly clear picture of the method of involvement of the cavernous sinuses.

As far as a careful study of the literature goes, there has never been a case of streptothrix infection reported as having had its origin in the external ear.

The two most completely worked out cases are those of Eppinger and Löhlein. Both started as pulmonary conditions, and later by metastatic ways produced multiple brain abscesses. The infection of the great brain sinuses by this organism seems to be unknown.

The congenital absence of the antrum in our case is certainly very suggestive, and at the same time the extraordinary displacement forward of the sinus, to within a few millimeters of the external bony canal, leads one to the enticing theory that the infection of the right sigmoid sinus was by direct contiguity. This is borne out by the fact that one of the most characteristic pathologic features of a streptothrix infection is its so-called perforative tendency. If, for example, a small area of the pleura is involved, it may pass directly through the chest wall and give rise to an external abscess. With such a well known clinical tendency, we can well assume that the process started in the middle ear in early childhood, and by a slow process of ulceration broke down the few millimeters of protecting bone between it and the abnormally placed sinus, and then by the long contact with the wall of the sinus started the thrombotic process. The absence of the antrum, noted at the time of the operation and later confirmed at autopsy, would be additional proof that the process was always confined to the middle ear until later in life. The reason why the patient never received treatment for his condition was because the mastoid was never involved, and the sinus trouble was the first serious complication which he experienced.

It is also to be noted that the fever curve was at all times remarkably low for a sinus complaint of such magnitude and apparent degree of purulent degeneration, and the very few attacks of chills would seem to indicate that a streptothrix infection of the sinuses does not give rise to such marked symptoms as does a streptococcus infection. Of course, the subsequent microscopic examination with the continued absence of true bacteria clearly explains why the very turbid spinal fluid gave no bacterial content. It was of course not

examined for streptothrix at the time, as the condition was not then ever remotely suspected.

The condition of the cavernous sinus and the post- and periorbital tissues showed how impossible any satisfactory operative procedure would have been. The capsule of the orbit was so tense at the autopsy that when a puncture was made with a knife the pus spurted out under pressure. In this connection it is interesting to note how very slight were the changes observable with the ophthalmoscope.

It does not seem in place in this paper to discuss the various operative measures for attacking the infections of the cavernous sinuses. It would seem that the autopsy proves that in such a case as this operative procedure would have been worse than useless.

The autopsy findings, however, give us a certain right to theorize on the possible method by which the infection of these sinuses took place. In the diagrammatic figure shown in figure 1, the shaded parts shows the extent of the involvement. The fuller details were noted by me at the time of the autopsy for the specific purpose of tracing the mode of infection of the cavernous sinuses, and do not appear in the necropsy report of Prof. Ophuls.

The most striking thing about the appearance of the sinuses was the fact that two kinds of thrombi could be distinguished, which in all probability were different stages of the same process, but still distinct enough to show in which direction the thrombotic process was extending. First, there was the thick, yellow, semifluid purulent thrombus, which filled the right transverse, the right sigmoid, the right bulb and part of the upper part of the right jugular. About one inch from the torcular, or at the point that the operation was ended and free bleeding commenced, there was a reddish thrombus, that looked somewhat like a postmortem clot, but with greater consistency.

The purulent type extended up the right superior petrosal, did not seem to involve the inferior petrosal, invaded the sinus cavernosus and by way of the sinus circularis Ridleyi involved the whole region in a fluid purulent mass. From here the infection extended to the periorbital tissue, turning then into bags of pus under great pressure. The same purulent process now descended the left superior petrosal, involved the left sigmoid, where the purulent type was halted. The left trans-

verse and the left bulbar region were again filled with the reddish, nonpurulent clot.

It seems fair to assume then that we have to deal here with a cavernous sinus involvement of originally otitic origin, the infection extending upwards along the right superior petrosal against the stream and then downward with the stream to the opposite side.

The careful bacteriologic examination of Prof. Ophuls would seem to indicate that the infection was a pure streptothrix infection, with the addition of very few if any real pus organisms. The preoperative bacteriologic examination would seem to substantiate this condition.

BIBLIOGRAPHY.*

52. Foulerton: The Pathology of Streptothrix Infections. Allbutt's System of Medicine, Vol. 2, Part 1, p. 302.
53. Horst: Zeitschr. f. Heilkunde, 1903, Vol. 24, p. 157.
(Full literature to date.)
54. Petruschky: Handbuch der pathogenen mikroorganismen. Edited by Kolle and Wassermann, 1903, Vol. 2, p. 832.
55. Engelhardt and Löhlein: Zur Kenntniss der Streptothrix-pyämie. Deutsches Archiv. f. klin. Med., Vol. 75, 1903, p. 112.
56. Rosenbach: Ueber das Erysipeloid. Archiv. f. klin. Chirurgie, Vol. 36, 1887, p. 346.
57. Eppinger: Ueber eine neue pathogene Cladothrix und durch sie hervorgerufene Pseudotuberkulosis. Ziegler's Beiträge zur pathol. Anat., Vol. 9, 1891, p. 287.
58. Armquist: Zeitschr. f. Hygiene, Vol. 8.
59. Buchholtz: Zeitschr. f. Hygiene, Vol. 24.
60. Chiari: Zeitschr. f. Heilkunds, 1900.
Cohn: Biologie der Pflanzen, Vol. 1, Heft 3.
61. Cozollino: Zeitschr. f. Hygiene, Vol. 33.
62. Ferrari: Wiener klin. Wochenschr., 1899, No. 36.
63. Ferre and Faquet: Erg. d. allg. Path., Jahrgang 3, 1896.
64. Flexner: Centralblatt f. Bacteriologie, Vol. 24, p. 83.
65. Forster: Archiv. für Ophthalmologie, Vol. 15.
66. Fuchs: Vers. d. ophth. Gesellsch., 1896.
67. Garten: Zeitschr. f. Chirurgie, Vol. 41.
68. v. Graefe: Archiv. f. Ophth., Vol. 15.
69. Gruber: Archiv. f. Hygiene, 1873, Vol. 16.
70. Hesse: Deutsche Zeit. f. Chirurgie, Vol. 34.
71. Krause: Münchener med. Wochenschr., 1902, p. 749.
72. Löhlein: Münchener med. Wochenschr., 1902, p. 1161.
73. Naunyn: Mitteilungen aus der med. Klinik zu Königsberg.
74. Norris and Markin: Jour. of Experimental Med., Vol. 5, No. 2.
75. Riviere and Sabarez: Erg. d. allg. Path., Jahrgang 3, 1896.
76. Rosenbach: Archiv. f. klin. Chirurgie, Vol. 36.
77. Rullmann: Münchener med. Wochenschr., 1898, 1899, 1902.
78. Scheele and Petruschky: Congress f. innere Med., 1897.
79. Silberschmidt: Centralblatt f. Bacteriologie, 1900.
80. v. Schroeder: Klin. Monatblät. f. Augenhellkunde, 1894, 1896.

*The complete bibliography of this subject can be found in the above-mentioned article of Foulerton, up to 1906, and will not be repeated here. He gives 51 references, and the numbers in this article will continue from that number on, thereby giving a complete bibliography to date, April, 1913.

81. Tschierschke: Inaugural-Dissertation, Breslau, 1891.
82. Lubarsch: Ztschr. f. Hyg., Vol. 31, p. 187.
83. Schabad: Ztschr. f. Hyg., Vol. 47, p. 41.
84. Löhlein: Ueber Gehirnabszess durch Streptothrix. Münch. med. Wochenschr., 1907, p. 1523.
85. v. Ritter: Ueber einen fall von durch eine Streptothrix bedingter Pleuritis ulcerosa mit metatatischer Gehirnabszess. Prager med. Wochenschr., 1900, p. 525.
86. Claypole: On the Classification of the Streptothrices. Journ. Exp. Med., Vol. XVII, No. 1, 1913.
87. zur Nedden: Klin. Monatblät. f. Augenheilkunde, 1907, p. 152.
88. Hoffman: Gangrene of the Outer Ear Due to Streptothrix. Ztschr. f. Ohrenhkde., Vol. 51, 1906.

Diagram of the Sinuses. From Brühl's "Diseases of the Ear."

1. Bulbus oculi, with distended pus sac.
2. Vena ophthalmica, enormously distended.
3. Sinus cavernosus.
4. Sinus circularis Ridleyi.
5. Sinus petrosus superior.
6. Sinus sigmoideus.
7. Sinus lateralis.
8. Venæ jugularis.
9. Bulbus venæ jugularis.