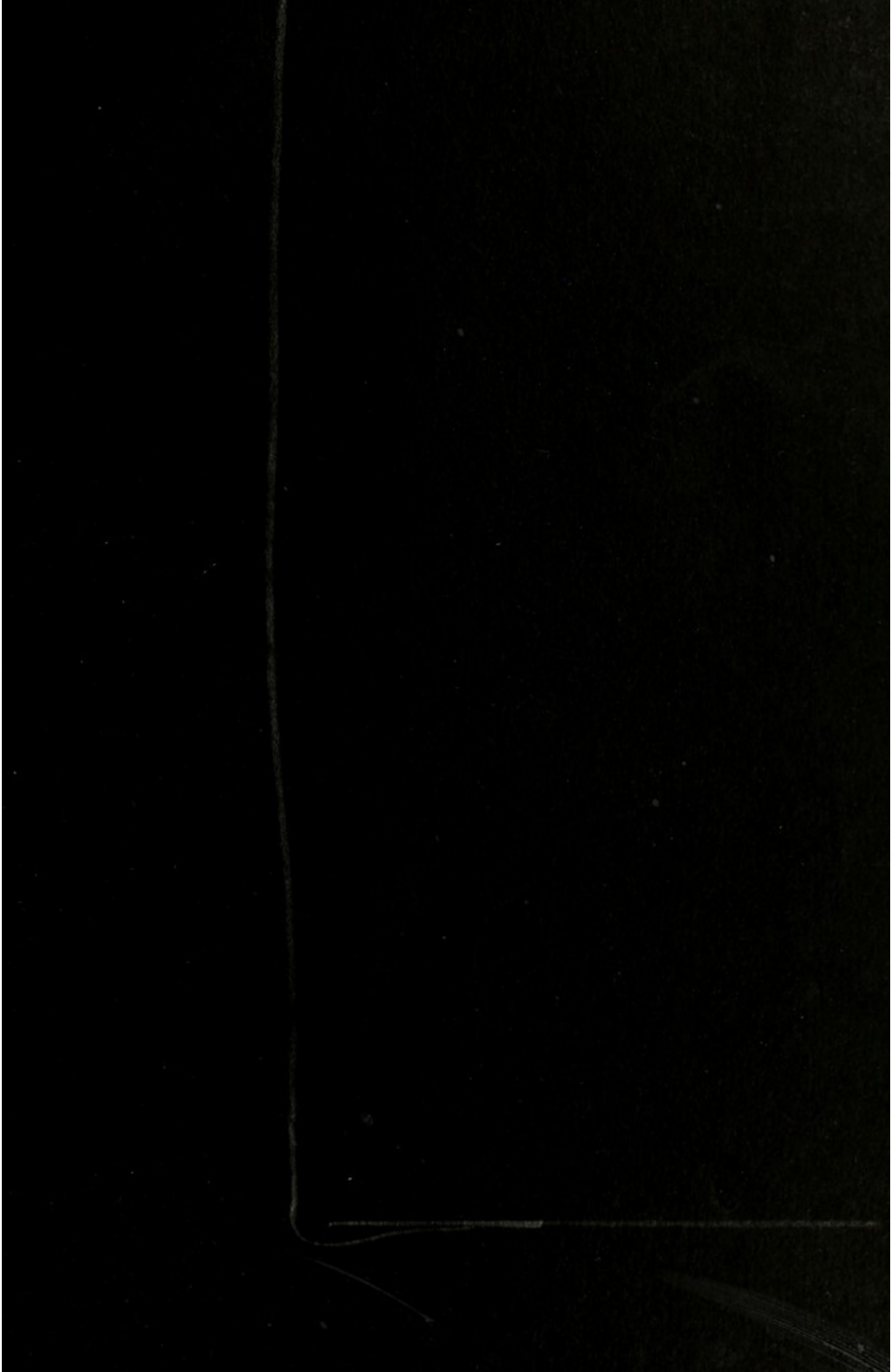
Exothalmic goitre : lesions of the cervical ganglia / by R. Shingleton Smith.



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LESIONS OF THE CERVICAL GANGLIA

BY

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(With Lithographic Drawings.)

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EXOPHTHALMIC GOÎTRE:

LESIONS OF THE CERVICAL GANGLIA.

The following paper is intended to supply a record of a typical case of Graves's disease, in which, after death, definite lesions of the cervical sympathetic system—both coarse and microscopic, the one affecting one ganglion only, the other affecting all the cervical ganglia—were observed. No attempt is made to elucidate the whole pathology of the disease; the absence of any information as to the cerebro-spinal nervous system impairs the value of the case, excepting from the one point of view, the implication of the sympathetic system.

Margaret W., aged twenty, domestic servant, was admitted to the Bristol Royal Infirmary on October 11, 1877, with a condition of well-marked exophthalmic goître. Very little history could be elicited from her beyond the fact that the symptoms had been of seven months' duration, and were first noticed a short time after her marriage. From the patient's mother the following facts were gathered:—That the daughter had manifested shortness of breath for years, and that she "always had large eyes"; that she had been engaged for twelve months, and was fairly well at the date

of her marriage (March 31, 1877); that after the marriage she had a great deal of anxiety, had lived with her husband only six months, and during that time had twice left him, and "made it up again"; that she had menstruated twice after her marriage, but not again since; that three years before she had amenorrhœa for several months; that a month after her marriage her eyes were noticed to be more prominent than formerly, she complained of feeling ill, and went to the infirmary at Cardiff, and here it was noticed that some "swelling of the throat" existed; that for a month before the marriage the mother had noticed a "dirty colour" of her daughter's face, and that at same time she once had an attack of palpitation, which lasted all night, but did not incapacitate her from work on the following day; that she had been getting thin ever since the marriage, but had not complained much of palpitation; that she was formerly of an amiable disposition, but since her illness had become irritable and quick-tempered.

No family history of nervous disease could be gathered. The father was invalided home from the Crimea with heart disease, but is still living. The mother is a thin, weakly-looking woman, but seems well. There are no brothers or sisters.

Her condition on admission was as follows:—A weakly-looking, emaciated girl, looking older than the age given, with very prominent eyeballs, enlarged neck, dusky face, complaining of palpitation with much dyspnœa, and vomiting. The eyeballs were equally prominent, both showing a considerable band of sclerotic all round the cornea; the insertions of the recti muscles could be seen; on closing the eyes, about a quarter of an inch in vertical width remained uncovered. The conjunctivæ were much injected, tears overflowed on the cheeks; large tortuous veins could be

traced over the sclerotic, giving it a dusky aspect. The neck was found to measure fourteen inches in circumference around the centre of the thyroid enlargement. Both thyroid lobes were enlarged equally; very large tortuous arteries could be traced along the surface of each lobe, and an arterial thrill could be felt and heard over these distended vessels. The whole face was markedly cyanotic, but there was no marked distension of the cervical veins. The heart-pulsations were 140 per minute; the pulse was small and weak. Nothing abnormal could be detected on auscultation—heart and lung sounds were normal. Tongue was blue, and slightly coated. Urine had a specific gravity 1015, acid, clear, light-coloured, no albumen, no sugar. She was ordered ext. belladonnæ gr. $\frac{1}{4}$, in pil., every four hours.

On October 14 the vomiting was much worse; it gave rise to considerable lividity of face, and there was marked dyspnœa. Pulse 140. She had slept fairly, in fact, was unnaturally drowsy. Was ordered liq. atropiæ ♏iij., hypodermically, night and morning, and to take an effervescing draught every four hours.

On October 18 the vomiting had subsided, and the pulse had come down to 120.

On October 20 pulse again 140. The eyes did not seem to protrude so much, and the neck measured thirteen inches and a half. She was much depressed in spirits; would cry and sob violently without reason, and at other times would break out into hysterical laughter.

On October 21 her face was much less dusky; there had been no more vomiting. Pulse 120.

There was little variation from day to day till the 29th, when the pulse was 156, very small and compressible. She complained of headache and of feeling very hot. The pupils had not become dilated, and she had not complained of thirst.

The atropine was continued from the 14th to the 31st; at first it gave great relief, as it seemed to allay the vomiting, relieve the dyspnœa, and slow the pulse, but the effect was evanescent, and it was therefore discontinued. Ext. ergotæ liquidæ in drachm doses three times a day was ordered.

November 1.—Pulse 136; she complained of not feeling so well. The eyes appeared to be less prominent than before. She was able to get up, and to sit up the greater part of the day. The neck measured thirteen inches.

24th.—Pulse 136. She felt pretty well, and was in good spirits. Neck thirteen inches and a quarter.

December 2.—Pulse 104.

14th.—Pulse 120. Neck twelve inches and a half.

19th.—Not so well. She was more emotional and excited; eyes more prominent. Neck thirteen inches and three-eighths. Pulse 136. Was ordered tinct. digitalis ℥x. every four hours.

23rd.—She complained of dyspnœa and of cough; expectorated glairy mucus, not blood-tinged; had been sick again. Pulse 160.

24th.—Pulse about 180; vomiting frequent; was ordered the atropine hypodermically as before.

25th.—Pulse was counted at 208. The eyes were more prominent. She seemed very weak, and had a troublesome cough, but there was no accumulation of fluid in air-passages.

26th.—Pulse was 160, and she felt better; was ordered pulv. digitalis gr. iss. every four hours.

28th.—Pulse 140. She was extremely feeble, and took little nourishment; still complained of dyspnœa, and the cyanosis had much increased. Laryngotomy was performed, but it gave no relief; the pulse rose and was several times counted over 200, but very small and weak. Death occurred

about an hour after the operation on December 29, at 12.45 p.m.

Post-mortem Examination, twenty-three hours after Death.—The body was small and much emaciated. Skin slightly jaundiced. Eyes still prominent, but less so than before death. Rigor mortis absent. Thyroid gland enlarged bilaterally and equally; each lobe was about three inches in vertical length, and two inches antero-posteriorly; laterally it was an inch and a half in diameter. Its surface was markedly lobulated over the whole convexity, especially at the upper and lower extremities, where definite, almost isolated, nodules were seen to project. The surface, looking towards the middle line of the body, was deeply concave for the trachea, around which the two lobes closely fitted, the groove for the trachea passing from above downwards and obliquely backwards. On cutting into the gland it was found to have a loose, spongy texture; no spaces or cysts were visible, and no fluid escaped, but the surface of the section was divided up by bands of areolar tissue continuous with and prolonged from the fibrous enveloping capsule into lobules about one-eighth of an inch in diameter. The trachea was slightly flattened by lateral pressure, the antero-posterior diameter being enlarged; but there was no actual obstruction or anything to impede the free passage of air. The lungs were much congested, and there was some consolidation of both lower lobes. The right cavities of the heart contained pale coagula; the right auricle was distended; the left cavities and the heart fibre appeared to be healthy. The liver was slightly enlarged from congestion; the spleen was also large and firm. The renal and uterine structures did not present anything abnormal. The brain was not examined. The sympathetic ganglia of the neck were removed for subsequent examination. They were placed

in chromic acid solution (half per cent.), and allowed to remain two or three weeks. The superior and middle ganglia presented no abnormality visible to the naked eye, but the inferior ganglion of the left side could not be found. The cord from the left middle ganglion was traced downwards, and was seen to spread out over a small gland-like swelling adhering to the left side of the trachea. This swelling occupied exactly the position of the inferior cervical ganglion, but no nerve-fibres could be traced beyond it. The nodule was of an oval shape, but flattened on the side towards the trachea, and intimately connected with the trachea by dense fibro-cellular tissue; it measured half an inch vertically and quarter of an inch laterally. Its surface consisted of dense fibrous tissue, into which the nerve-fibres were traced. This capsule measured about one-tenth of an inch in thickness. Internally was a hard calcareous substance forming a small calculus, the nucleus of the nodular mass. The calcareous mass consisted chiefly of carbonate of lime, with an organic matrix; fragments of it dissolved to a large extent, giving off bubbles of gas when treated with dilute acid. A few crystals of cholesterine were seen amongst the granular organic *débris* left undissolved by the acid.

Microscopic Appearances.—a. Thyroid: This gland presented a condition of vascular and villous hypertrophy. The circular spaces which exist normally were not enlarged, no cysts were visible, and there was no colloidal degeneration of the epithelial lining. The spaces were occupied by villous growths, the result of vascular and epithelial proliferation of the walls of the loculi. The villous projections were covered and the locular spaces were lined by a single layer of epithelium of the flattened columnar variety. *b.* Sympathetic Ganglia: Those ganglia which were found and could be

examined were ascertained to present similar appearances. Sections were made by the freezing process of both the superior, both the middle, and the right inferior ganglion. The nerve-structures were alike in all; the degree of vascularity and the connective-tissue element did not present abnormalities. In all there was a definite fibrous capsule, with fibrous septa running through the substance of the ganglion. In all of them the neuroglia element presented numerous nuclei, but not more than are found in other ganglia presumed to be healthy. The nerve element, more particularly the nerve-cells, did, however, present a very striking and characteristic deformity. The true nucleated and nucleolated cells were visible as granular masses, for the most part stellate in form, surrounded by a clear space, outside which a distinct nucleated cell-capsule could be traced. The cells varied much in size: some of them filled about two-thirds the area of the space enclosed by the cell-capsule, others had retracted to such an extent that they appeared to occupy not one-tenth of their normal space; some still remained in direct contact with the surrounding cell-sheath, others had broken away entirely, and appeared to be free within the capsule. In most cases delicate processes could be seen to connect the granular protoplasmic mass with the surrounding neuroglia element. The space surrounding the cells was for the most part clear, and appeared to be occupied by the fluid in which the sections were mounted; but in many cases rounded, small, nuclear masses seemed to lie free, or almost so, in the space, or projecting into it from the cell-sheath. Small oil-globules were seen in the same position in a few cells. The nerve-fibres had a perfectly normal appearance, the multi-oval-nucleated grey fibres, and the axis-cylinder fibres could be readily seen in sections through either of the ganglia: the grey fibres showed best in longitudinal sections, the

axis-cylinders best in transverse sections. Particular attention was given to these fibres, in consequence of the observation of Poniklo (*Lancet*, February 23, 1878), that in five cases of diabetes there was an absence of the medullated bundles of fibres from the sympathetic system in the abdomen. In a fatal case of diabetes recently under the care of my colleague Dr. Waldo, there was no difficulty in the demonstration of the dark-bordered axis-cylinder fibres in the semilunar ganglion, in the splanchnic nerves, and in the superior cervical ganglion; there appeared to be an excess of the connective-tissue nuclei in the solar ganglia, but on comparing the sections with others taken from the solar plexus of a healthy man who had died by accident, and which were prepared in a precisely similar manner, no difference could be observed.

Remarks.—This case, interesting from a clinical point of view, derives its chief interest from its pathological aspects. Few cases are on record in which any very definite lesion of the sympathetic system has been connected with the symptoms of exophthalmic goître. In this case, however, a very manifest coarse lesion existed, which had given rise to the entire destruction of the inferior ganglion on the left side of the neck. Whether the morbid process commenced in the ganglion itself or in the surrounding structures—*e.g.*, a neighbouring gland—is difficult to decide; but it is clear that a morbid process had been going on in immediate proximity to this ganglion, and, as a result of this process, the ganglion tissue had been entirely destroyed, its place being occupied by an inert mass of calcareous matter and fibrous tissue. The fact that the calcareous mass contained a small amount of cholesterine may be taken as an indication that the mass may have resulted from a degenerative process occurring in diseased nerve-tissue; the amount of choles-

terine observed was, however, too small to warrant such a definite conclusion. The absence of any such change in the other ganglia, and, on the other hand, the absence of calcareous or caseous glands elsewhere, must leave us in doubt as to the essential nature of the commencing lesion, and as to the exact tissue involved. Whether any morbid process affecting a small portion only of the cervical sympathetic system may be considered as a sufficient cause of the whole train of symptoms present in Graves's disease, is open to question. Accordingly, we are not justified in assuming that this was the primary or even the most important lesion present.

In most of the cases where morbid appearances in the sympathetic system have been observed, the pathological condition has been one of sclerosis: an excess of connective tissue has given rise to a wasting of the nerve elements. Dr. Reith records a case of exophthalmic goître where this condition was observed (*Medical Times and Gazette*, 1865); Poniklo describes a similar condition in the sympathetic ganglia of diabetes (*Lancet*, February 23, 1878). In the case now published no such increase of the connective-tissue element and no increased infiltration with connective-tissue nuclei were apparent. The condition observed was one of true atrophic shrinking of the nerve-cells proper. Such a lesion of the cells, not in one ganglion only, but affecting all and equally so, may be supposed to give rise to such symptoms as exist in the disease under consideration. We must not, however, forget one important fact, viz., that the ganglia had been submitted to the prolonged action of a weak solution of chromic acid (one-half per cent.). This reagent is well known to have a powerful action on nerve-cells; it causes them to become granular and contracted. In the spinal cord and brain-tissues this contractile action of chromic acid on the

nerve-cells is not so manifest, but on the sympathetic ganglia of persons dying from various diseases the chromic acid has been found to give rise to a marked degree of contraction, similar in kind to, but less in extent than, that which was found in the ganglia of the exophthalmic goître patient. Why the chromic acid should act differently on the nerve-cells of different parts, may be a questionable topic, but the fact that it acts far more powerfully on the cells of the sympathetic than on those of the cerebro-spinal system has been shown by numerous observations. The action of the preservative and hardening agent on the ganglia may partially account for the appearances described; but, over and above the results of the chromic acid action, there must have been either a previous atrophic condition of the cells, or such a condition as would cause under the influence of the chromic acid a far more marked contraction than occurs in the cells when in their normal state. No such contraction occurs under the influence of Müller's fluid or of spirit: it would therefore be desirable in future observations to use one of those two fluids in preference to the chromic acid solution.

It would be interesting to inquire how it is that a condition of vaso-motor paralysis such as exists in this disease can depend on the same condition which gives rise to acceleration of the heart's action. Presuming that the atrophic state of the ganglion cells is an important factor of the symptoms manifested, one must argue that the cardiac nerves and the cervico-facial system of vaso-motor nerves are affected differently, that there results a paralysis of the "vaso-motor" set, and at the same time a stimulation or irritation of the accelerator cardiac nerves. No marked abnormality of the patient's pupils was at any time noted; they were always rather large, but equal, and sensitive to light. The lachrymal glands secreted very freely under

emotional influences, and no abnormality of the salivary function was noticed. The functions of the cervical sympathetic were accordingly perverted, but not destroyed: the vaso-motor paresis alone indicated a paralytic condition of the sympathetic; other symptoms would rather indicate a condition of irritation of the ganglion cells of the cervical system.

Little comment on the symptoms and course of the disease is needed. The emotional condition of the patient was quite in accord with the usual reports of this disease. Mental worry and emotional excitement were the most prominent etiological facts elicited; the patient was constantly at one extreme or the other—at one time laughing, at the other crying. Her tendency to crying and sobbing was so great that it interfered, to some extent, with the treatment. Attempts were made to pass the constant current through the cervical cords, but on each occasion such profuse crying, and consequently increased prominence of eyeballs, resulted, that more harm than good was done. Any emotional disturbance of this kind always increased the capillary engorgement of the head and neck, and was usually accompanied by increase of dyspnœa. Vomiting was a very troublesome symptom on several occasions, and it always took place when the other symptoms were at their worst; it did not seem to depend on any gastric condition, but was presumed to result from vascular cerebral disturbance. The dyspnœa was frequently extreme, but not accompanied by any laryngeal stridor. At the post-mortem examination the trachea was found to be only slightly compressed. No actual obstruction to the passage of air existed; hence it was presumed that this symptom also depended on vascular disturbance of the medulla oblongata. The immediate cause of death was probably the very great difficulty in the circulation arising from the unusually rapid action of the heart.

DESCRIPTION OF PLATES.

1. Superior cervical ganglion — left, showing the contracted cells, with their star-like processes, the connective tissue matrix, and the nerve fibres in section.

   × 300 diameters.

2. Superior cervical ganglion—right, transverse section.

   × 360 diameters.

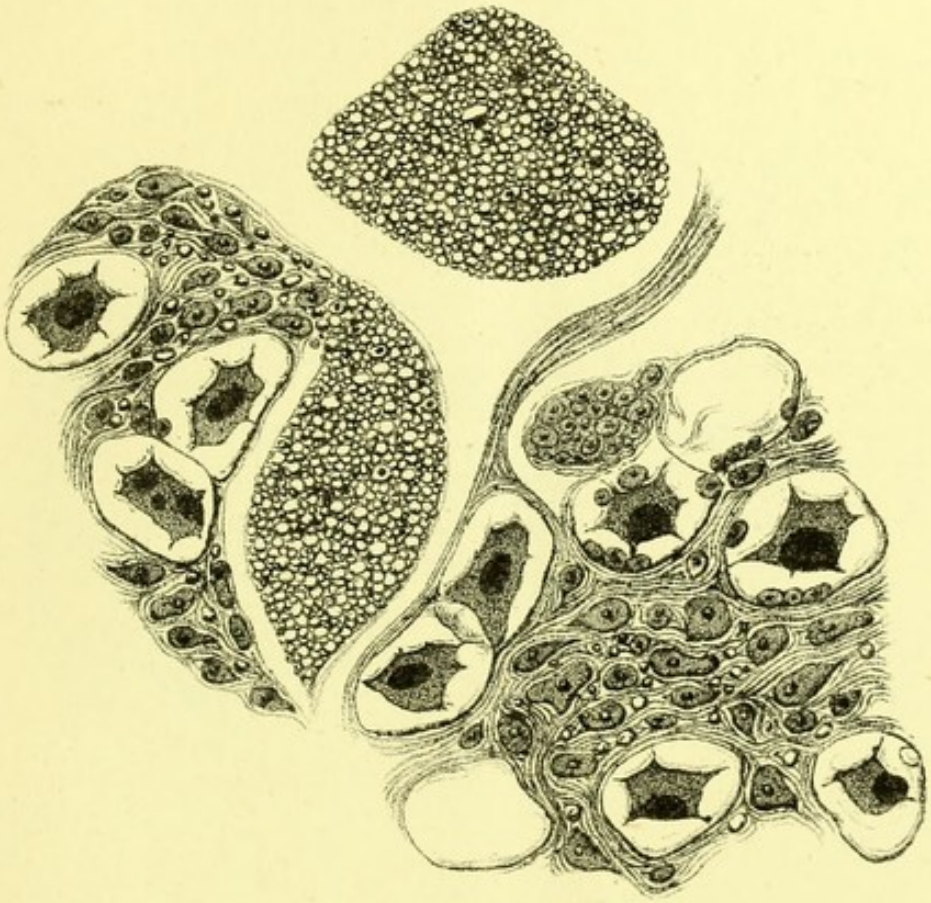
   Drawn by G. M. Smith.

3. Sympathetic cord in the neck, transverse section, showing the axis-cylinder and grey nerve-fibres, with connective tissue and vessels . . . . . × 300 diameters.

   Drawn by R. Shingleton Smith.

4. Thyroid gland, showing the villous processes projecting into the locular spaces, the epithelial lining, and the connective tissue nuclei . . . . × 200 diameters.

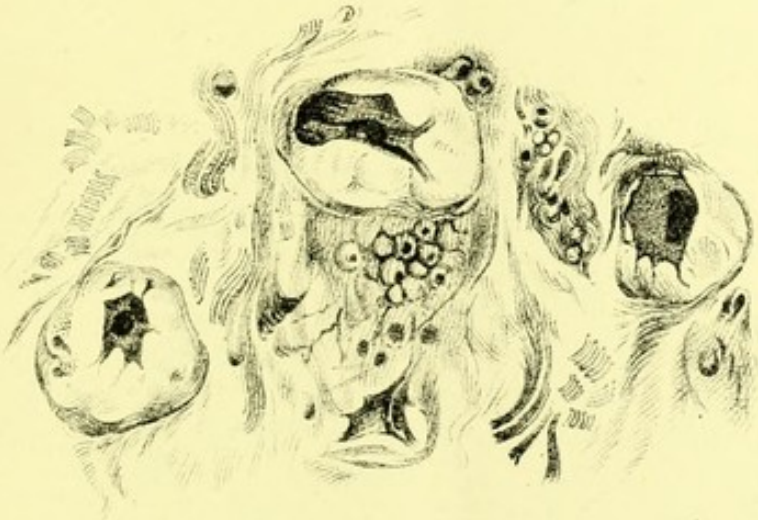
   Drawn by R. Shingleton Smith.

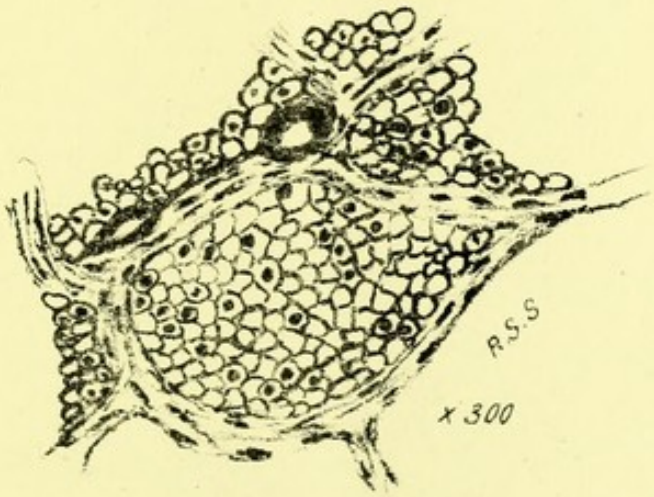


SUPERIOR CERVICAL GANGLION - LEFT -
TRANSVERSE SECTION.

× 300 diams

by Dr. J. Greig Smith.

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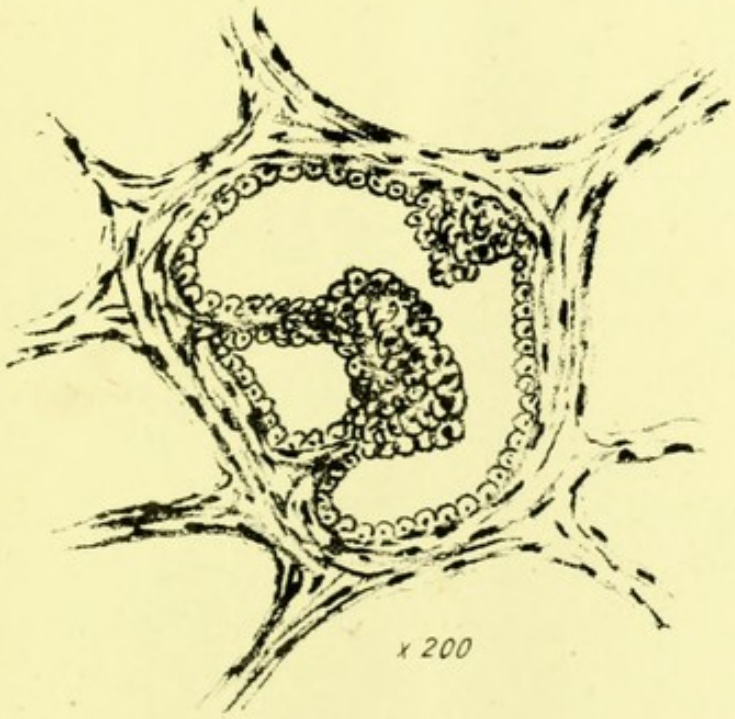

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