A CASE OF BILATERAL EIGHTH-NERVE TUMOURS ASSOCIATED WITH MULTIPLE NEUROFIBROMATA AND MULTIPLE ENDO- THELIOMATA OF THE MENINGES.

BY C. P. SYMONDS, LONDON.

THE following case is that of R. C. M., male, age 27, who was admitted to Guy's Hospital under Dr. Hurst on Oct. 23, 1920, for blindness, deafness, and inability to walk.

The History, which was obtained from the patient's wife, was that on his discharge from the Army in June, 1917, he was somewhat deaf, and complained of noises 'like a tramcar' in both ears. He also walked unsteadily, 'like a drunken man'. He suffered from severe headaches, especially in the early morning, and from dimness of vision in poor lights. The deafness progressed steadily, and by December, 1917, was absolute.

In March, 1918, he was admitted into a military hospital, where he was found to have organic nerve deafness with absent vestibular reactions, and it was also noted that he had absent ankle-jerks. The Wassermann reaction in the blood and cerebrospinal fluid was negative, but the diagnosis of tabes dorsalis was made as being the most probable explanation of this unusual combination of neurological signs. In July, 1919, his vision became much worse. In April, 1920, he began to complain of pain in the bottom of the back, and a few months later his wife noticed that in addition to the unsteadiness of his gait, long present, he showed a tendency to drag his feet when walking. The headaches became more severe, and were accompanied by vomiting. In September and October, 1920, he was a patient in an infirmary where the medical officer who looked after him noted: "His speech was, I thought, affected, being strongly suggestive of disseminated sclerosis; but his mother, with whom I have since had a talk, tells me his speech has always been slow and deliberate, and is not, in her opinion, altered". A later note adds: "His complete deafness makes investigation of his mental condition difficult; but, so far as I have been able to judge, it is little or not at all affected. In fact I have been struck with the intelligence with which he grasps a question one wishes to ask, or attempts to carry out a movement one wishes him to perform".

On admission to Guy's Hospital he complained of severe suboccipital headache, loss of sensation over the right side of the face and over the left leg, and pain in the back.

Examination was difficult, as the patient was almost completely blind and deaf, and greatly distressed by his headache. He could, however, be made to hear words shouted into his left ear, and by means of this and tactual sign language it was found that his mental condition was normal. He was able to give clear expression to his wishes, but his speech was halting and explosive, resembling that met with in disseminated sclerosis or cerebellar disease.*

He could distinguish between light and darkness with the right eye, but was completely blind in the left. The optic discs showed a high degree of papilloedema with secondary atrophy.

The right pupil reacted sluggishly to light: the left was inactive. Detailed examination proved tedious owing to difficulty in getting the patient to co-operate on account of his blindness and deafness. The following additional points, however, were established in the examination of the cranial nerves: left-sided ptosis and weakness of all muscles innervated by the left third nerve; absence of both corneal reflexes; weakness of the right face, especially of the lower half; protrusion of the tongue to the right.

There appeared to be some loss of sense of position in the left hand, and general loss of cutaneous sensibility of the left leg. All tendon-jerks in upper and lower limbs were absent, nor could the epigastric or the abdominal reflexes be elicited. The plantar responses were indefinitely flexor on the right; not obtained on the left. An attempt at flexion of the neck upon the trunk revealed considerable stiffness, and gave rise to complaint of pain. Kernig's sign was also present, and its elicitation caused severe pain in the lumbosacral region radiating down the backs of the thighs.

The Wassermann reaction was negative in the blood and cerebrospinal fluid; the latter contained 0 cells per c.mm., protein 0.04 per cent.†

A provisional diagnosis of acoustic-nerve tumour, probably bilateral, was made, and operation performed by Mr. Bromley on Oct. 30. The patient's condition at that time was extremely grave: during the five days preceding operation the temperature had been subnormal, the pulse-rate had risen from 80 to 110, and respiration was becoming steadily slower.

Suboccipital exploration revealed a tense dura, and when this

* I made this note before seeing those quoted above from the Infirmary records.

† Lumbar puncture was performed by the house physician before the diagnosis of a tumour in the posterior fossa had been considered.

was opened and the cerebellum exposed there occurred almost at once a gush of cerebrospinal fluid, which was followed by failure of respiration and death.

Post-mortem Appearances.—Apart from the changes in the skeleton and central nervous system, the only point of note was a moderate degree of mitral stenosis. (There is a doubtful history of his having had rheumatic fever when a boy.)

The Skeleton.—Skull: 5 cm. to the left of the lambda there is a bony mass projecting from the internal surface of the parietal bone. This is cone-shaped, with maximum height of 1 cm. and maximum diameter 2.2 cm.; 1.5 cm. above and to the right of the lambda on the internal surface of the right parietal bone there is a circular depression 1.5 cm. in diameter: this is roughly saucer-shaped, and in its centre the base is formed by a thin layer of periosteum only (*Fig. 1*). The internal auditory meatus on both sides is enlarged, especially on the right, and on this side

FIG. 1.—Inner surface of posterior part of calvarium, showing exostosis of left parietal bone and circular erosion of right.

a small portion of the acoustic-nerve tumour to be described broke off and remained in the meatus.

Other bones: No deformity of the thorax or vertebrae was noted. Both tibiae showed sabre-like bowing.

Meninges.—Over the left parietal lobe there is a deep depression corresponding to the bony projection in the skull, and at this point bone and dura were inseparable without the aid of a knife. Over the postero-superior surface of the right parietal lobe there is a small calcareous button growing from the outer surface of the dura, corresponding to the cavity of the skull at this point. The cerebral surface of the dura at this spot presents a punched-out hole 5 mm. in circumference, through which the tumour is adherent to brain substance; 1 cm. distant from this there is a small dome-shaped fibrous nodule in the substance of the dura. Overlying the foot of the left precentral gyrus there is another tumour growing from the internal surface of the dura. This is an irregular nodular mass, 3.5 by 2.5 cm. in its widest lateral dimensions, and 1 cm. in depth (*Fig. 2*). There are many small fibrous plaques scattered about the internal surface of the dura, which look as if they might be starting-points of other growths.

Brain.—Occupying the posterior part of the left parietal lobe, as shown in the photograph (*Fig. 2*), is a large solid tumour, the external surface of which is roughly circular and flush with the surface of the brain. In its centre is a depression corresponding to the bony projection of the skull referred to above, and at this point the dura is inseparable from the tumour. The diameter of the tumour is 6 cm., and it is situated in the area normally occupied by the supramarginal and angular gyri. It was readily enucleated from the brain substance, and then proved to be roughly hemispherical, as seen in the photograph (*Fig. 3*), its greatest depth being 4 cm. The contours of the neighbouring gyri are so much distorted as the result of pressure that it is not possible to determine their outlines with accuracy.

At the foot of the left precentral gyrus, and extending forward into the inferior frontal gyrus, is a depression measuring 3 by 2 cm., and 2 cm. in depth, corresponding to the tumour growing from the superjacent dura (*Fig. 2*). The anterior ascending ramus of the Sylvian fissure lies in the anterior wall of this depression, which therefore includes the intermediate and posterior parts of the inferior frontal gyrus.

At the base of the brain the cerebellopontine angle on either side is occupied by a nodular tumour the size of a small walnut (*Fig. 4*). On the right side the fibres of the seventh nerve are visible spread out over the inferior surface of the tumour. On the left side also some fibres apparently of the seventh nerve are seen on the surface of the growth. When the tumours are lifted aside, the lateral aspect of the pons on each side is seen to be deeply indented, and the trigeminal nerves are flattened by pressure.

Spinal Meninges and Nerve-roots.—Growing upon the inner surface of the dura are many hard plaques of a nature similar to those seen on the cerebral dura, but of a smaller size. There are also one or two similar nodules definitely arising in the arachnoid. The largest of these latter, the size of a split pea, appears to be almost free,

FIG. 2.—Lateral view of left hemisphere. The fissures of Sylvius and Rolando are rendered conspicuous by the insertion of strands of dark wool. In the precentral region a portion of the dura has been left intact and hinged back to show the tumour; below is the depression caused by it in the surface of the brain. The tumour of the parietal lobe has been replaced *in situ* after enucleation.

FIG. 3.—Lateral view of parietal tumour shown in *Fig. 2*, after enucleation (superficial aspect to the left).

being attached by very slender connections to a slip of the ligamentum denticulatum. Upon almost all the nerve-roots there are small fusiform swellings of the type usually known as neurofibromata. There is one nodular swelling much larger than the others (2 cm. in diameter) growing from one of the upper sacral roots on the right side and compressing the conus medullaris and the neighbouring nerve-roots (*Fig. 5*).

The outline of the left lateral surface of the cord is interrupted at the eleventh dorsal level by the projection of a round nodule which appears to lie beneath the arachnoid (*Fig. 5*).

The Peripheral Nerves.—During life

FIG. 4.—Base of brain, showing acoustic tumour in each cerebellopontine angle.

The eighth-nerve tumour shows the microscopic appearances characteristic of these growths. The area examined consisted mainly of a loose reticular formation, the cells having small round nuclei and irregular stellate cytoplasm. There are also strands of densely-packed cells with oval nuclei and slender fusiform cytoplasm which show a tendency to arrangement in whorls. These cells do not take up the fuchsin of Van Gieson's stain, but remain a brownish-yellow, in contrast with the bright pink of the blood-vessels and capsule of the tumour. Many of the vessels show great thickening and hyaline degeneration.

The sections of the tumour of the cauda equina show very much the same structure, with the addition, however, of many scattered areas in which the fusiform cells show the palisade arrangement of nuclei illustrated in Cushing's monograph.¹

Longitudinal sections through the small posterior-root tumour show

no subcutaneous tumours were observed of the type met with in von Recklinghausen's disease, but at the post-mortem Dr. Ryle discovered a small nodule apparently growing from one of the subcutaneous nerves of the right leg. This was taken for histological examination, but was unfortunately lost.

Microscopic Examination.—

Sections were cut of the tumour growing from the left eighth nerve, of a small nodule from one of the posterior nerve-roots, of the nodule described as arising from the arachnoid of the ligamentum denticulatum, and of the larger tumour situated upon the cauda equina. Sections were also cut from the inner surface of the large left-sided parietal tumour, and from the edge of the nodular growth of the dura in the left precentral area. Transverse sections were made of the cord in the mid-dorsal region, and at the point where the subarachnoid nodule referred to above lay upon its surface.

this to be composed of fusiform cells of similar appearances and staining reactions to those described above.

The sections through the tumour lying upon the surface of the cord prove this to be another growth of similar type, developing apparently from posterior-root fibres, and at one point invading the substance of the cord along the line of the posterior horn of grey matter. Here the strands of advancing fusiform cells are surrounded by a marked increase in glia-cell formation. The appearances are almost identical with those figured by Bassoe and Nazum² and by Bruce and Dawson³ in similar cases.

The structure of the dural tumours is that of the so-called endotheliomata. They are composed of oval or spindle-shaped cells with a definite tendency to whorl formation and calcification, and the resultant appearance of psammoma bodies. The cells lie in closely-packed masses in a frame-work of connective tissue and blood-vessels which takes on the characteristic pink colour with Van Gieson's stain. In the section from the edge of the smaller tumour, finger-shaped processes of these cells are clearly seen invading the under surface of the dura in a manner which reminds one of a basal-celled carcinoma.

It proved impossible to cut the arachnoid nodule without preliminary decalcification. It is almost entirely composed of psammoma bodies, in the outer walls of which occasional cells are to be seen of similar nature to those seen in the dural tumours.

A section through the cord at the mid-dorsal level stained by the Kulschitzky-Pal method shows some degeneration of the fibres of the posterior columns, presumably secondary to the posterior-root destruction at lower levels.

Symptomatology.—The main points in the symptomatology of eighth-nerve tumours are well known, especially since the publication of Cushing's monograph¹.

In his series one case is recorded in which the presence of bilateral deafness and multiple cranial-nerve palsies led to a diagnosis of bilateral acoustic neuroma, whereas there was found after death a single large tumour on the left side, with great distortion of the pons and other structures at the base. It is of some interest to note that in this case of Cushing's there was paralysis of both third nerves, a condition for which he finds it difficult to give a satisfactory explanation. In the case recorded above, the paralysis of the left third nerve gave rise to some difficulty in making the diagnosis, but is probably to be explained as being due to the degree and duration of increased intracranial tension; in Cushing's case also the history covered more than two years, and total blindness had resulted from secondary optic atrophy. The third-nerve palsy

FIG. 5.—Lower part of spinal cord with meninges and nerve-roots. For description see text.

therefore is to be regarded as one of those late 'false localizing signs' which, as Collier¹ has shown, often occur in the presence of greatly increased intracranial tension, adding much to the difficulties of diagnosis.

Against this, standing out in the background of the picture, is the early history of tinnitus and deafness—facts which were only elicited by close questioning of the patient's wife, but were of the highest value in arriving at the diagnosis. Cushing¹ has emphasized the constancy of these subjective troubles of hearing and their invariable occurrence at an *early stage* of growth in cases of eighth-nerve tumours.

It is interesting to note that in this case some degree of hearing was preserved in the left ear long after vestibular reactions had been lost. This is in accord with the view of Henschen⁵, that these tumours arise primarily from the vestibular rather than the cochlear root. In point of fact in this case, as in one reported by Biggs⁶ and another by Bassoe,² the larger tumour was on the side on which hearing had been retained. It is therefore of interest to note that the right-sided tumour in this case was at its apex so firmly embedded in the internal auditory meatus that this fragment of it was broken off in removal, whereas on the left side the tumour came away from the bone quite easily. It would seem possible that the degree of deafness depends upon the tightness with which the cochlear root is wedged against the walls of the bony canal.

Passing to the symptoms of pressure upon surrounding nerves, those referable to the trigeminal are in accord with the general rule that pressure exercised upon the sensory *root* (i.e., proximal to the Gasserian ganglion) causes anæsthesia—not pain. On both sides the trigeminal root was flattened out between the tumour and the pons. The sixth nerves had, as usual in tumours of this type, escaped direct pressure. Unfortunately no note was made of the functional efficiency of this pair, but my impression is that the left eye was entirely paralyzed for outward as well as inward movement. The sixth nerve, perhaps on account of its long course, is frequently paralyzed when intracranial tension is extreme.

There is some doubt whether the facial weakness on the right side should be attributed to direct pressure upon the nerve or to the effects of the dural tumour pressing upon the left precentral cortex. Probably the latter is the correct interpretation, since the tongue also was weak on the right side without any obvious wasting. It is at any rate remarkable that such a degree of distortion of both seventh nerves should be accompanied by no more definite signs of facial palsy.

In relation to the large tumour pressing upon the cauda equina,

the most interesting point is the loss of ankle-jerks, which preceded by a long time the appearance of pain severe enough to be a prominent feature in the story. The absence of sphincter disturbances also is of interest.

On the other hand, the history was incomplete, and both root pains and loss of sphincter control may have existed at some time and have been accepted as signs of tabes.

In the later stages of the illness the absence of all tendon-jerks was presumably due to the break in the reflex arcs occasioned by the presence of the multiple tumours upon the posterior nerve-roots.

The two endotheliomata shown in *Fig. 2* are, on account of their situations, of some interest in relation to problems of the localization of speech centres in the brain. The smaller tumour had produced a considerable indentation of the cerebral surface in precisely that area in which Broca and his many followers have found that a superficial lesion will give rise to paresis of verbal utterance. The larger tumour had burrowed deeply into those parts of the parietal and temporal lobes which are considered to be of functional importance in the reception of speech and in the elaboration of intellectual processes in terms of speech.

The problems of aphasia have been recently reviewed in this country by Head⁷ and others⁸; and in France Marie and Foix⁹ have reported in detail the results of studies of aphasia following gunshot wounds of the cortex in correlation with anatomical localization of the lesions. In these papers there appears to be nothing to contradict the general statement that, in the case of a right-handed person, a lesion in either the posterior part of the inferior frontal convolution or in the supramarginal and angular gyri in the left hemisphere will give rise to disturbance in the former situation of outgoing speech and in the latter site of incoming speech.

It has been ascertained from the relatives of this patient that he was always right-handed in everything he did. On the other hand, it is to be regretted that he was not more carefully examined from the point of view of speech disturbance. He certainly had some difficulty in vocal utterance, the words being widely spaced and blurted out with undue effort. This was set down at the time of examination as being due to interference with the co-ordinating functions of the cerebellum. It may, however, have been a minimal sign of motor aphasia. In any case it was insufficient to have attracted the attention of his wife or mother.

On the receptive side one may say, with certainty that there was no gross disturbance of speech recognition. Provided one shouted loud enough into his left ear, he was quick to obey any command or answer any question, however complicated. A further point of

interest is furnished by the fact that the sister in charge of his ward was an expert in tactual sign language in which the patient had been trained, and was able to ask him questions in this way. Not only was he able to appreciate the individual letters correctly, but he showed a high degree of facility in guessing the whole of a word from the first few letters, or the whole of a sentence from the first few words, according to the context. It was noticeable that he always used the left hand for the reception of these tactual messages.

Marie and Foix's⁹ observations show that lesions of the supra-marginal and angular gyri are generally accompanied by 'global' aphasia and apraxia; and Bremer¹⁰ has recently published a case in which the same clinical picture was caused by an endothelioma which in size, shape, and situation closely resembled that seen in the present instance. What, then, is the explanation of the relative absence of speech disturbance in the present case?

It may be that the extracortical tumours of slow growth, such as the endotheliomata, cause relatively little damage to the brain in spite of their great size. Evidence of this kind is furnished by the very complete recovery which patients make when these tumours are removed at operation, showing that what damage there is, is not of a permanent nature. In Bremer's case referred to above, the patient had almost completely recovered from a very severe degree of aphasia a month after his operation.

An alternative hypothesis that may be tentatively put forward in this case rests upon the theory of 'stock-brainedness'. Foster Kennedy¹¹ has collected a group of cases showing that in a right-handed person coming of left-handed stock the speech centres may be situated on the right hemisphere instead of the left. Inquiry in the present case has elicited the fact that the patient's paternal grandmother was left-handed, but that all other members of the family in the present and past generations are right-handed. It is thus barely possible that the patient, being a right-handed person, yet had his speech centres located in the right hemisphere.

Pathology.—The association of bilateral eighth-nerve tumours with multiple neurofibromata of the central and peripheral nervous system is well known, and, although it is a rare condition, many cases have now been recorded, of which those reported and illustrated by Bassoe and Nazum² and Hall and Beattie¹² are typical examples. There are, furthermore, several cases on record in which the co-existence of multiple endotheliomata of the meninges has been noted. Cushing,¹ in a brief review of the literature upon this point, concludes that generalized neurofibromatosis, isolated tumours of the eighth nerve, and fibro-endotheliomata of the meninges are in some fashion correlated lesions. He says "it would seem probable that some

anomaly of development of the nervous system and its envelopes must be the underlying factor". He assumes that the endotheliomata and the neurofibromata are "obviously of an utterly different pathological character".

On the other hand, Greenfield,¹³ describing the histological appearances of a tumour of the occipital cortex in a case of this type, concludes that, although in many respects resembling an endothelioma, it is more closely allied to the other tumours (neurofibromata) of the series.

In the present case the microscopic appearances of the two sets of tumours are quite distinct, and lend support to Cushing's view. The cells of the nerve tumours are uniformly more elongated and slender than those of the dural growths. The former show no tendency to the formation of psammoma bodies, in which the latter abound. And whereas in the former there is very little connective tissue (pink staining with Van Gieson's stain) except immediately around the vessels, in the latter there is a distinct fibrous framework.

As to the nature and origin of the nerve tumours, every aspect of this problem has been most fully discussed by Durante¹⁴ and in the detailed histological studies of Bruce and Dawson.³

Cushing¹ and Greenfield,¹³ in recent reviews, both favour the hypothesis that these tumours arise from the cells of the neurilemma or sheath of Schwann, which originally develop from the neural crest. On this assumption, in spite of the superficial resemblance of these growths to young fibrous tissue, there is no justification for the appellation fibroma, and the term neurinoma coined by Verocay¹⁵ would seem to be more suitable.

The microscopic appearances and staining reactions of the cells of this series in no respect differ from those reported by other observers, and the picture of slim fusiform cells invading the cord in the posterior-root-entry zone shows a striking similarity to that of Plate VI, Fig. 53, in Bruce and Dawson's work.³ As they remark, "it seems as if the neurilemma sheath in relation to the posterior roots were continued along the fibres right into the root-entry zone".

Bony Deformities.—The forward bowing of the tibiæ in this case was not assigned any importance in making the diagnosis, but there seems to be little doubt that it should be connected with the presence of multiple neurofibromata. Marie and Couvelaire,¹⁶ in a detailed record of a case of generalized neurofibromatosis, drew special attention to the skeletal changes, which in their case were confined to the thorax. The bones were soft, flexible, and light, so soft that "on a pu modeler à sa guise ce bizarre thorax". They remark upon the likeness of the bone condition to that met with in osteomalacia, and quote other observations by Jeanselme¹⁷ and Hoisnard.¹⁸

One of Jeanselme's¹⁹ cases is said to have shown a *sabre-like deformity of the right tibia*. Lion and Gasne²⁰ reported a similar case in which, in addition to the thoracic deformity, there was an enlargement of one ulnar bone, in the centre of which an x-ray plate showed an area of decalcification. They also refer to a case described by Raymond in which there was similar deformity of the humerus.

Pearce Gould,²¹ writing in 1918 upon the bony changes occurring in von Recklinghausen's disease, declares that skeletal deformities are among those constantly to be found in addition to neurofibromatosis. He further quotes a statement (without reference) to the effect that they occur in a degree noticeable during life in about 7 per cent of all cases. In one of the cases which he examined he found that all the bones were soft and cut easily with a knife, and microscopical sections showed the presence of much osteoid tissue with little calcification. He concluded that the histological picture was that of osteomalacia, rather than that of osteitis fibrosa or simple decalcification. The patient from whom the tissues were taken is said to have had an exaggerated knee-jerk and Babinski's sign on the right, but there is no post-mortem report upon the nervous system. I have not been able to find in the literature any instance in which bony changes are described in a case of central neurofibromatosis without subcutaneous tumours, but there seems to be no reason why they should not occur.

My acknowledgements are due to Dr. A. F. Hurst for permission to publish the clinical notes of this case, and to Dr. P. P. Laidlaw for much assistance and advice in the preparation of the photographs.

REFERENCES.

- ¹ CUSHING, H., *Tumours of the Nervus Acusticus*, Philadelphia, 1917.
- ² BASSOE, P. and NAZUM, F., "Report of a case of Central and Peripheral Neurofibromatosis", *Jour. Nerv. and Ment. Dis.*, 1915, xlii, 785.
- ³ BRUCE and DAWSON, "Multiple Neuromata of the Central Nervous System", *Trans. Roy. Soc. Edinburgh*, 1913, xlviii, part iii, 697.
- ⁴ COLLIER, JAMES, "False Localizing Signs in Cerebral Tumours", *Brain*, 1904, xxvii, 490.
- ⁵ HENSCHEN, F., "Zur Histologie und Pathogenese der Kleinhirnbrückenwinkel-tumore", *Arch. f. Psychiat.*, 1915, lvi, 21.
- ⁶ BIGGS, G., "Case of Multiple Intracranial Tumours with involvement of both Auditory Nerves", *Lancet*, 1909, ii, 14.
- ⁷ HEAD, H., "Aphasia", *Brain*, 1920, xliii, 390.
- ⁸ DISCUSSION on Aphasia, *Brain*, 1920, xliii, 412.
- ⁹ MARIE, P., and FOIX, CH., "Les aphasies de guerre," *Revue neurol.*, 1917, xxiv, 53.
- ¹⁰ BREMER, F., "Global Aphasia and Bilateral Apraxia due to an Endothelioma comprising the Gyrus Supramarginalis", *Arch. of Neurol. and Psychiat.*, 1921, v, 663.
- ¹¹ KENNEDY, FOSTER, "Stock-brainedness, the Causative Factor in the so-called 'Crossed Aphasias'", *Amer. Jour. Med. Sci.*, 1916, cliii, 849.

- ¹² HALL, A. J., and BEATTIE, J. M., "A Case of Diffuse Neurofibromatosis", *Proc. Roy. Soc. Med., (Path. Sect.)*, 1912, v, 140.
- ¹³ GREENFIELD, J. G., "Pathological Examination of Forty Intracranial Neoplasms", *Brain*, 1919, xlii, 29.
- ¹⁴ DURANTE, J., "Nerfs", *Cornil and Ranvier's Manuel d'Anat. patholog.*, 1907, iii, 425.
- ¹⁵ VEROY, "Zur Kenntnis der 'Neurofibrome'", *Beitr. z. path. Anat. u. z. allg. Path.*, 1910, xlviii, 1.
- ¹⁶ MARIE, P., and COUVELAIRE, A., "Neurofibromatose généralisée", *Nouv. icon. de la Salpêtrière*, 1900, xiii, 30.
- ¹⁷ JEANSELME and ORILLARD, "Contributions à l'étude des malformations congénitales de la peau et de l'hypoderme", *Rev. de Chir.*, 1894, Jan., 50.
- ¹⁸ HOISNARD, "Contribution à l'étude de la neurofibromatose généralisée", *Thèse de Paris*, 1898.
- ¹⁹ JEANSELME, "Etude histologique sur un cas de maladie de Recklinghausen", *Soc. de Derm. et de Syph.*, 1898, Nov. 10.
- ²⁰ LION and GASNE, "Maladie de Recklinghausen", *Bull. Soc. méd. Hôp. de Paris*, 1904, xxi, 5.
- ²¹ GOULD, ERIC PEARCE, "The Bone Changes occurring in von Recklinghausen's Disease", *Quart. Jour. Med.*, 1918, xi, 221.