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The patients who appeared to derive some benefit were cases I., VI., VIII., and XVII. Cases I., VIII., and XVII. were very similar in symptoms, in all three refusal of food being the greatest difficulty to combat, and in all there certainly was some improvement in this respect after the attempts at hypnotism, but the results gained would appear to have been due much more to the large amount of personal attention devoted to each case than to any hypnotic influence. Case VI. was not in a condition of stupor as were the other three, and if suggestion had any effect, it was suggestion without hypnotism.

Cases XI. and XXI. were certainly hypnotized. In case XI. further experiment was prevented by her removal from the hospital, but the suggestion made in the very light hypnotic state induced was not acted upon.

Case XXI. promised well at first, but further experiment failed. Suggestions seemed at first to be in a very small degree successful, but instead of the effect increasing it rather rapidly diminished.

We do not pretend that these failures dispose of the question as to the possibility of treating the insane in England by hypnotic suggestion. The cases are merely narrated as evidence of an honest attempt to make a trial in an English hospital for lunatics of a method of treatment which is said to have been successful abroad. Whether English patients can be hypnotized as easily as those of other races is a question. The amount of time and care spent in these cases has been very considerable, and so far the results are not encouraging for further attempts at present. It would be a matter of satisfaction to know whether other English observers have arrived at similar or other results, but at present we know of no report of such cases. We hope that hypnotism will be given a fair trial in other hospitals and asylums in England, and that others may meet with more success than we have done.

CLINICAL NOTES AND CASES.

The Morbid Histology of a Case of Syphilitic Epileptic Idiocy. By F. St. JOHN BULLEN. Pathologist to the West Riding Asylum, Wakefield. (With plate.)

Dr. Judson S. Bury has narrated several interesting cases illustrative of the influence of syphilis upon the production of idiocy, with important comments ("Brain," April, 1883), and to his quoted instances I venture to append another.

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It is unfortunate, however, that a family history was unobtainable, inasmuch as other factors, such as intemperance, epilepsy, etc., could not be excluded, thus limiting the causal agency to syphilis. Nevertheless, taking into account the actual evidence of the disease in the brain and the gross constitutional infection, that it was the most potent, even if not the sole, originating influence, is probable.

From the conditions revealed by the microscope in the examination of the cortex cerebri, there is but little doubt that the defect of mind was congenital; the impress of this was on the brain-cells at their birth, independent of any subsequent evil effect through endoarteritis, meningitis, or sclerosis.

The histological features in this case are in some respects especially interesting as exemplifying the condition of nervecell and nucleus vacuolation found in connection with epilepsy. This constant pathological substratum of the disease, which has been discovered by Dr. Bevan Lewis and fully described by him in his "Text Book of Mental Disease," I, through his kindness, have had the great advantage of recognizing for the past three years, and during that period have had sufficient opportunity, not only to corroborate the truth of the morbid appearances described, but to appreciate the important deductions made by him in connection with them.

The subject is so fully dealt with by Dr. Lewis, that in virtue of the similarity of the changes found in the present case, I have not chronicled the characteristic appearances so much in detail as they admit of. Moreover, as the lesion is not a rare nor isolated one, but on the contrary to be seen of all observers, there is no need to do more than direct attention to its main features. The changes in the cortex in this case are not more marked than usual, and indeed, by no means as pronounced as at times manifested.

As this paper is going to press, I see that a more recent observer, Dr. J. R. Whitwell, has made investigation into "nuclear vacuolation in nerve-cells." His original article ("Brain," January No., 1890) will be of interest when viewed as confirmatory of the account given of the lesion by Dr. Bevan Lewis, who has also divined the true pathological significance of the morbid change.

G. P. Admitted August, 1885, into Wakefield Asylum. Died February, 1889, æt. 16 years.

No information was obtainable, except that convulsive seizures

commenced about the age of three years, and that a brother is believed to be an idiot.

The boy was an idiot of very low type; quite unable to utter any articulate sound, and almost completely devoid of intelligence. He would manifest signs of pleasure when taken notice of, but understood nothing spoken to him; when handled in the course of examination, struck passionately about him and screamed. The mere sensations of vision and hearing appeared unimpaired, pictures and coloured objects evoked manifestations of delight, although obviously conveying no meaning to him.

The physical features were, briefly, these: Light hair and blue eyes. The right cornea almost universally opaque through interstitial keratitis, most dense in the centre, so that the pupil behind could not be seen; apparently anterior synechiæ were present. Vision, seemingly, quite lost in this eye. The left pupil fully dilated.

The cranial contour not especially noticeable. On the left side of the forehead, a remarkable oval depression of the brain-case, about oneand-a-half inches by a quarter to three-quarter inches, the long axis upwards and outwards; the depth at centre, a quarter inch; margins sharply defined, floor shelving from frontal bone above. At the external inferior angle an aperture existed, filled with pus, fluctuating synchronously with the heart pulsations, and during sleep, with the respirations only. A depression of similar form, but of less extent, was placed at the vertex of cranium, just in front of the interauricular line and a little to the left of the median suture. This depression had a hard, firm floor, and no discharging sinus was present.

The bridge of nose was not sunken. Teeth exceedingly crowded, irregular, and carious, many pegged and notched, especially the upper incisors, in the most typical manner; those of the lower jaw, though crowded, were not irregular. The gums spongy, and bleeding on the slightest pressure; palate unduly arched; lips thick and everted. Skin, generally, over body of a peculiar coppery hue.

Fingers long and slender; those of left hand usually were flexed on the palm, and the hand on the wrist, the condition appearing one of clasp-knife rigidity. Voluntary overcome of the latter was only most slightly possible; when the fingers were extended forcibly they became locked in that position until somewhat bent, when flexion into the palm again occurred. The same condition existed to a small extent at the elbow.

The right arm and hand were used almost entirely for feeding himself, etc. Both upper extremities equally nourished. Erect posture or locomotion were impossible, as the right lower limb was paralyzed and the seat of contractures; the leg flexed on thigh, and thigh upon abdomen, extension only to be performed to a very slight extent. Marked amyotrophy in right limb as compared with left existed. Movements in the latter free, but voluntary actions very disorderly, and muscles most feeble. Plantar and patellar reflexes, normal; the superficial not obtained. Cutaneous sensibility everywhere unimpaired. Cicatrices from burns (?) on throat and thigh.

Fits occurred about three or four times a week, for the first year. All the limbs were convulsed, and strongly so. On one occasion it was noted that blood oozed out of the frontal depression during a fit. During the next twelvemonths the seizures increased in frequency from one to three or four in the twenty-four hours, and so remained, excepting for a period of two days, on each of which six occurred, only arrested finally by chloral. Both lower limbs at last contracted. On several occasions sustained fractures of clavicle, humerus, and lower part of femur; the bones being so extremely brittle that it became necessary never to move him from one bed to another. Grew very feeble and emaciated. Always negligent in habits.

Autopsy.—Trunk appearances: Much emaciation. Contractures of lower extremities and left upper, as depicted in illustration. Moderate left lateral spinal curvature. Old united fractures in left humerus, right ulna (two), upper end of left femur, and false joint at middle of right femur. Several nodes on humeri and femora, also on front of left tibia.

No especial appearances in trunk-viscera.

Cranium.—The skull presents over about the middle of the orbital ridge of the left frontal bone an irregular aperture, about one-and-aquarter inches long by one-third to half-an-inch wide; the long axis directed upwards and outwards. The edges of this are jagged and bevelled from without inwards, and there is some deposit of new bone at its margins. To the latter, the underlying dura is adherent. There is another area on the left side, about half-an-inch from the sagittal suture, its posterior edge lying about two inches from the coronal suture, its anterior, three-quarters of an inch; of ovoid shape, occupied almost entirely by new hard osseous tissue, conjoined by serrated margin to a peripheral ring of older bone, the latter itself affixed to the main mass of the parietal bone by irregular dentations.

The dura mater forming the floor of the aperture in the frontal bone is much thickened by dense white fibrous bands, and roughened; it is stretched tightly across the opening, making a pretty firm and resistant occluding lamina. The superior longitudinal sinus is empty and of narrow calibre.

The soft membranes are thickened by exudation, except over occipital regions, and in parts are areas of dense opacity so caused, and there is some slight clouding along the course of most of the vessels in the fronto-parietal regions. The basal vessels are of ordinary arrangement, but much thickened and showing patchy dense opacity, which in the left-middle and both anterior cerebrals becomes pretty general, or in lengthy segments.

The pia covering in the *lamina perforata antica* is raised up by a large ovoid swelling, the size of a big walnut, and formed by the in-

fundibulum, which is distended by the evident great excess of ventricular fluid into a sac with delicate grey membranous walls and tense fluid contents. By this swelling the optic commissure is far pushed out from the base of the brain.

Previous to stripping the membranes, the brain weighs 1,355 grammes, is somewhat wasted-looking, and wanting firmness. On tapping the fluid swelling at the base, serous liquid to the amount of fourteen ounces escapes, and the organ becomes flattened and sunken at vertex and very pulpy. The internal membranes, corresponding to the site of aperture in the frontal bone, are slightly adherent to the dura, but are not torn on removal from it. Here, also, they are thickened more than elsewhere, and have a rough, hard feeling, almost as if a thin plate of bone lay beneath. No attempt at separation from the brain-cortex in this region is made, for fear of spoiling future microscopic observations. Over certain parts of the vertex, viz. : posterior ends of second and third frontal and summits of central gyri, on the right side, and the latter position on the left, stripping the membranes leaves well-marked erosions of the cortex, the superficial layer of which, in small portions, is occasionally firmly incorporated with them. These lacerations are confined to the summits of the gyri, and resemble those found in general paralysis, though not, for the most part, so deep. No tubercular deposits appear in the pia when microscopically examined, nor do the capillaries show evidence of disease in, or morbid products around their coats.

The frontal lobes do not present any obviously notable contour; both are, however, composed of very coarse and symmetrically-running convolutions; decidedly below average complexity. The insular gyri are, too, very simple; the left shows the three hinder digitations fused into one large fan-shaped mass, with furrowings indicative of the normal divisions.

On the right side the entire angular gyrus, with the adjoining (only) portion of the supra-marginal and hinder end of the first temporosphenoidal convolutions, is wasted, shrivelled, and sclerosed. No pulpy condition exists, either superficially or deeply. The cortex is of somewhat yellowish hue, and the diseased gyrus passes quickly, but not abruptly, into its continuing convolutions. On slicing across the angular no very noticeable macroscopic change is obvious, beyond extreme thinning of the cortex and narrowing of the medullary core. At the root of the latter there is certainly an excessive number of very coarse puncta, but these exist throughout the occipital region of this (and the left) side, together with an increase in the generally-lessened consistence of the white substance, although in no way approaching to actual ramollissement. The medullary substance between the cortex and ventricles is everywhere much thinned by the great distension of the latter. The corpus callosum is so diminished in thickness and consistence that it tears under the most gentle manipulation of the brain, as does, also, the soft pulpy medullated lamina representing the fornix.

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The basal ganglia are seen much flattened out. In both corpora striata an oval-shaped area of depression exists on the ventricular aspect at the junction of the head and tail. A division of the substance at one of these sites shows lessened consistence and dusky coloration of the brain matter by numerous very coarse vessels.

The whole of the right cornu ammonis is of extreme gristly hardness and toughness; the left cornu is only slightly increased in firmness.

The optic nerves are firm and of normal contour; their transverse section 3×4 mm. The right shows an apparent inner dark area, denoting some degeneration. There is no coarse appearance of disease in the optic tracts, as indicated by discoloration or wasting, and the quadrigeminal bodies seem in no way affected.

The ependyma of lateral and fourth ventricles is very granular. The depth of cortex in the following regions is: Left asc. frontal, 3.75 mm.; right asc. frontal, 3 mm; right angular, 1.5 mm; left frontal (beneath aperture in bone), 1.75 mm.

Motor Region.—In certain portions of this the field shows an unusually sparse distribution of stained elements, both neurine and interneurine; as regards the former, not taking into account those cells unchanged or partly destroyed only, but including all apparent, in any stage.

A very striking number of the pyriform cells of the third stratum present well-marked vacuolation, both of nucleus and protoplasm. Of the two the former is the most frequent site by far. In this, all stages of the diseased process are seen, from the appearance of a tiny, brilliant speck in the nucleus to the almost complete disappearance of the same, a narrow, deep-stained ring, representing the circumferential part, alone remaining—or its entire absence, a mere hollow shell of protoplasm being left.

Vacuolation of the protoplasmic investment is especially well seen in the cells of the ganglionic formation. Occasionally several large vacuoles surround the nucleus, which appears, as it were, supported on the remaining filaments of protoplasm, like a stone in the claw-setting of a ring. According to the position of these, the nucleus is displaced, entire, to one or other side or corner of the cell, or is broken up, or, again, maintains its usual site. Most of the ganglionic bodies show far advanced disease; some are obtusely rounded, swollen, granular, and have imbibed the aniline dye until the protoplasm is hardly differentiable from the nucleus. Some, on the reverse, are so faintly stained that they seem scarcely demarcable from the intercellular tissue. Either of these kinds may have a highly-stained and, perhaps, unusually large nucleus, or the latter may seem absent. Large pigmentary accumulation exists in others, causing marked bulging of the cell, and in more than one instance rupture at this point has occurred, and a mass of pigment lies partly or wholly discharged, in the latter case leaving a hollowed-out cell, with or without one or more clearly defined vacuoles. Others in this region are quite spherical, with stunted processes, the basal often alone remaining.

In the nucleus of these large cells vacuolation commences, frequently in three, four or five places, and proceeds until nothing but a circular rim remains, or the nucleus breaks up into segments. There are, besides the foregoing morbid changes, a large proportion of cells in the third stratum, which are altered in one way or another; being, perhaps, globose, or irregularly bulged with pigment, and often extremely pale and ragged-looking, the nucleus much atrophied, or even not apparent. The protoplasmic extensions of these cells are not only very feebly stained, but short, rough, and often broken off.

The second and claustral strata have not escaped. In the first, vacuolation is frequent, and a good proportion of the nerve elements are in various morbid conditions, up to that preceding removal; in the last, vacuolation is a prominent feature in the nucleus, and is the most noteworthy one. There is some difference in the character and amount of the degeneration found in parts of the motor area. The immediately-preceding changes have been described from sections taken from the five-laminated cortex at the summit of the left ascending frontal gyrus. Sections procured from the corresponding locality on the right side show uniformity in kind, but less intensity. Those from the summits of both ascending parietals present vacuolation comparatively quite seldom, and morbid changes, altogether, are not very obvious. The pyriform cells of the third layer, and especially the deeply-placed ones, are thickly studded with nucleated cells, whilst capillary vessels, or lines of cells indicating their course, are numerous. On the other hand, the first-described changes are not associated with any perceptibly-increased vascularity; indeed, rather the reverse obtains.

Antero-frontal Region .- Sections carried through those portions of the first and second frontal gyri subjacent to the aperture in the frontal bone show the normal structure, both grey and white, of the second frontal to be obliterated as to its histological features, the tissue substituted extending across the intervening sulcus into the core of medulla of the superior frontal. The pia is firmly welded to the cerebral cortex through the extremely coarse belt of neuroglia in the first stratum, nearly all of which last is somewhat darkened by the increase of connective. The histological characters of the replacing tissue are not everywhere similar. The portions entrenching upon the claustral layer of the first frontal gyrus present a dense overgrowth and hyperplasia of connective-tissue corpuscles, but no discoverable cell accumulation in the meshes formed by their ramifications. Yet more towards the medullary core angular and rounded cells are seen fairly closely arranged in these spaces, and amongst which run many capillary vessels. Some of these are nervous elements. Elsewhere found, and passing up to the cortical surface of the second frontal gyrus, where it blends with the peripheral belt of neuroglia, is densely

fibrillated connective tissue, running in thick sheave-like bundles, and totally eclipsing every trace of nervous structure; whilst patches of still deeper staining denote the especial aggregation of fibrous tissue around vessels.

Cortex of First Frontal Gyrus.—The arrangement of the stained elements in this region appears somewhat crowded, by reason of the large number of nucleated cells, mapping out the course of capillaries and free in the neuroglia. A general aspect, also, of irregularity is given by the inequality of staining, resulting from the different stages of disease affecting the nerve cells, by, to some extent, morbid variations in their shape, and by the presence of numerous fragmentary remains of the same.

Of the more specialized changes, the most prominent are in the pyriform cells of the third stratum. In great part these are shrunken; in a fewer number, on the reverse, swollen or globose. In all alike the protoplasmic extensions are badly, or even not seen, and in many instances the cell body is so pale and ill-defined that but for the deepstained nucleus these elements would hardly appear other than faint circumscribed darkenings of the neuroglia basis. There, is, however, a morbid change which picks out these pyriform cells notably, and, in some degree, is present in a large proportion of them, and that is vacuolation of the nucleus, seen in all stages. It may be stated that where the nerve elements in the third layer do not show this, it is because the nucleus is not to be seen, and may presumably have succumbed; the cells themselves are but faded remnants, evidently in the final stage of decay; the protoplasm appears to have suffered independently of the nucleus, and lastly and seldom, because the cells show no alteration.

The same quality of change exists in the other nerve-cell strata, though not so marked, nor so general.

It has been already mentioned that numerous capillaries are indicated by tracts of nucleated cells, and a great excess in the number of vessels, visible as such, ramify throughout all the cortical laminæ. This hypervascularity probably is in connection with the deep-lying connective-tissue overgrowth.

Sites of Meningo-encephalic Adhesion.—Here is found very marked thickening of the peripheral neuroglia, from which, at parts, extends downwards, through almost the whole depth of the first layer, a tolerably dense fibrillation. Elsewhere, in the same regions, active scavenger-elements are present numerously. But with this exception, and the occasional appearance of a very small group of these latter corpuscles amongst the cells of the third stratum in the antero-frontal cortex, no notable increase of connective tissue is found in the cortical laminæ. It is indicated that the large ganglionic cells of the motor area are distinctly more degenerated deep to the sites of marked sclerosis in the peripheral zone.

No changes whatever are obvious in the occipital region. The

right angular gyrus throughout its entire depth has its proper structure replaced by an exuberant growth of connective-tissue elements. The affection appears to be a genuine sclerosis.

Cornu Ammonis.—In the stratum of the large pyramids exists an excess in the number of nucleated cells, both pericellular and free in the neuroglia; from this cause the field appears more closely dotted with stained-elements than usual. The former hide not only the outline of the cell, but often its entire mass, packed in grape-like clusters, and lying seriatim along the apex process. These overlain cells, and many of the others, seem of much impaired vitality, are, where in view, pale and poorly stained, the nucleus occasionally vacuolated, the apical process retracted, ill-defined, or unseen, so that, en masse, much of the characteristic superincumbent radiation is lost.

The pyramidal cells rapidly thin out below the conjunction of the lamina medullaris externa with the fascia dentata, and disappear for the whole of the inrolling almost, until the hilus fasciæ dentatæ is reached, when a few indistinct cells come again into view. Their vanishing is absolute in some sections; in others a few degenerated elements alone represent.

It is hardly necessary to say that the actions from which the preceding and following descriptions are made were chosen from a site in which the continuance of the pyramidal layer around the fascia dentata is either not at all, or but for a very short distance, interrupted.

In the area bounded by the convolute of the granule layer is seen, under a low objective, a great excess in the number, with considerable distension, of the capillary vessels over those found in the normal state. Variously contorted, they traverse the field in all directions ; their walls are generally closely sprinkled with branching nucleated More highly amplified, the latter show their pale protocells. plasmic investment, and the delicate filament which joins them from the lymph-connective cell in the vicinity. At these points the adventitial sheath is, not seldom, pulled-out laterally. The so-called spider cells are in great abundance and plainly seen, even under a low power, their processes ramifying far and wide. Their tentacular extensions can occasionally be perceived attached to nerve cells, which show changes in shape and substance indicating their progressed disorganization. The whole of the lamina medullaris externa of the subiculum cornu ammonis presents a darkening, due to increased connective-tissue formation; and in the stratum reticulare not only general coarseness of the neuroglia exists, but the vessels are thickly overlain and surrounded by connective-cells, forming quite dense clumps, their numerous extensions contributing a closely-fibrillated aspect around.

Much the same description applies to the alveus, and large branching cells lie in the neuroglia layer just outside the stratum

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granulosum. As it has been seen that the pyramidal cells have almost vanished, and their site is only represented by an abnormally dense and deeply-stained band, it would appear that some degree of sclerosis has taken place pretty generally throughout the ammonshorn. Further, a thick and close belt of neuroglia forms the boundary on the ventricular aspect. In the perfectly fresh state (immediately after cutting on the 'ether-freezing microtome, and before staining even) this zone was crowded with colloid bodies, which are, however, but faintly visible now. There are yet other changes in the gyrus hippocampi to be noticed, and these are:—The very obvious affection of the cells constituting the clump-formations of the subiculum, by vacuolation, mostly nuclear; and the remarkable prevalence and high degree of the same morbid appearance amongst the grouped pyramids of the gyrus hippocampi.

Sites of wasting in Corpora Striata.-The position of these has been roughly indicated already; they are approximately opposite to the anterior pillars of the fornix; are exactly symmetrically placed, and nearly as equally apportioned as to area and degree of degeneration. The tissue of the caudate body, on each side, immediately contiguous to the ventricular wall, for about 0.75 c.m. outwards, and extending about 1.5 c.m. vertically, has undergone degeneration. Macroscopically, in place of the compact parenchyma, little more than a framework of connective tissue remains at this site, the neurine substance around being soft and friable. No coarse signs of hæmorrhage or ramollissement appear in the vicinity. Under the microscope is seen the following :- Near the borders of the focus of degeneration there is well-marked moniliform segmentation of the medullated fibres, which proceeds at times almost to isolation of the segmented portions of Schwann's white matter, but, for the most part, a notable varicosity prevails. A cloudy appearance of the tubules is common, and pretty universally, but a certain accompaniment of the segmented medullary masses, nucleated cells, lie along the course of the nerve-fibres. The protoplasmic investment of these cells is often quite plainly seen, even in the hardened sections, whilst infrequently branches are observed spreading out over the medullated tube. These latter cells are present in great number, and especially in the neighbourhood of capillaries are aggregated almost in mass. Here, again, patches of deep-stained, fibrillated connective replace in limited areas the proper nervous tissue. Α rather free permeation by vascular channels is apparent, as indicated by linear tracts of nuclei, as well as by the vessel tunics themselves, which present also, frequently, a notably beaded contour. The larger capillary trunks in this region have their muscularis thickened and nuclei over-numerous, and in the largest-sized vessels, where cut transversely, there is a decidedly thickened intima and free proliferation of the nuclei.

As the focus of degeneration is encroached upon, the nerve-tubules

gradually drop out of view, and, partly no doubt owing to the replacement of them by connective-tissue, and in part to the process of preparation, are almost absent. Where seen, they are granularlooking, and have absorbed diffusely the staining-reagent. A mesh-work of fibrous strands remains, dotted with a quantity of nucleated cells, and interspersed with capillaries, granule-masses, etc.

Sections taken through the mesencephalon, pons, medulla, and spinal cord, in various regions, show no recognizable disease in the course of the motor tracts. And, moreover, excepting the following site, no lesion appears in any portion. Only in the vicinity of the sylvian aqueduct is degeneration found; here, at the front, and laterally of the aqueduct, is there much thickening and condensation of the neuroglia, and in the former situation, as far forwards as the oculo-motor nuclei, there is a large number of freely-branching connective-tissue cells. The nerve nuclei and roots seem normal, nor is lesion found in the remaining areas of the section. Both internal capsules are stained by carmine, and after Pal's method, but no degeneration is discovered.

In the lumbar cord, the investing pia is somewhat thickened, congested, and the seat of a considerable cell-exudation around the larger vessels. The anterior nerve-roots are quite healthy-looking.

The optic nerves and chiasma present no morbid change.

Cerebral Tumour involving the Frontal Lobes. By A. HILL GRIFFITH, M.D., Surgeon to the Royal Eye Hospital, Manchester, and T. STEELE SHELDON, M.B.Lond., Cheshire County Asylum, Macclesfield.

Jessie P., aged 23, was a nurse at the Parkside Asylum.

She was a tall, well-developed, handsome girl, with brown hair and irides, and of clear pale complexion. Several members of her family had died of phthisis, and the father was rheumatic, but the patient herself showed no symptoms of tubercle and had not suffered either from rheumatism or from scarlet fever; there was no history and little probability of the acquisition of syphilis, and no injury to the head had been sustained. Menstruation had always been scanty.

She first consulted Dr. Griffith on the 9th December, 1886, but there had been these symptoms preceding: Severe left-sided neuralgia and occipital headache, accompanied with nausea and vomiting, had occurred in paroxysms during several months; occasionally there was nocturnal delirium, and she complained at times of temporary dulness of vision and hearing, especially in the morning; there was some impairment of memory, and she was losing flesh; hysteria seemed to afford sufficient explanation of the symptoms until the development of

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