A CASE OF CHRONIC PROGRESSIVE CHOREA WITH ANATOMICAL STUDY.

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Notwithstanding the copious literature which has accumulated during recent years regarding the affection, chronic degenerative chorea is still quite an obscure disease. This is especially true in respect to its etiology and pathology.

In reference to the etiology of the disease little is known, and, although homogeneous heredity appears to be a pertinent factor in many instances, it fails to explain the origin of the disease in the first diseased ancestor. Typical cases have been reported in which the absence of heredity could be established. It is therefore evident that other factors are to be considered, and, in consequence, some writers, Schabad, Westphal and others, have assumed the possibility of its connection with pregnancy, shock, migraine, etc.

Careful studies in the pathology of this disease are of great interest and importance, as the determination of its morbid anatomy will assist in elucidating the pathology of other diseases associated with choreiform features. It would therefore appear expedient that all cases of chronic progressive chorea should be thoroughly studied clinically, and, whenever possible, pathological investigations made.

Following is a report of the history and pathological findings in a case of Huntington's chorea, being one of three cases of this disease in which the writer has made pathological studies during the past year.

J. W., aged 33, was admitted to the Government Hospital for Insane on August 25, 1909, and died April 1, 1913.

Family History.—Father and mother were natives of England. Father died at the age of 87 years, was of good habits, and at no time showed any evidence of nervous or mental affection. Mother died at the age of 78 years, as a result of chronic gastritis. She had always enjoyed good health up to the time of her final illness, and was not regarded as in any way nervous. The patient was the fourth child of a family of six children,

consisting of three girls and three boys. All of his sisters and brothers are still living and in good health. Special care was taken to ascertain whether any indication of the disease occurred in his antecedents, but no such instance could be determined.

Personal History.—Patient was born in England, and when an infant was brought to this country by his parents, who settled in New York. With the exception of measles at the age of ten years, his childhood and boyhood were normal. He entered school at the age of seven years and continued through one year of high school, showing a good scholastic record. At the age of 17 years he left school and began the study of music under a cornetist. Subsequently he enlisted in the army as a first class musician, and served eight years. He at no time indulged in the use of alcohol or drugs, and never suffered from any venereal diseases. While serving in the army he contracted dysentery, and was ill for about two months. He was married when 23 years old; his wife had no children or any miscarriages.

History of Present Illness.—In the spring of 1905, about four years before the patient entered the hospital, he suffered with symptoms of nervousness. A few months later involuntary muscular movements became manifest, causing his fingers to move and his hands to start; at the same time his arms became affected. About a month later his legs began to show some shakiness. At this stage of the disease the movements were temporarily controllable on voluntary effort.

The jerking of his legs became so pronounced that his gait simulated that of a drunken man, and, before his wife appreciated the nature of the disease, she frequently accused him of being intoxicated. Upon consulting a physician, he was informed that he had chronic chorea.

The involuntary motions increased in severity, and in consequence he was forced to give up his vocation entirely. He made application for a pension, which was granted. In the course of the next few months his facial muscles became involved and his speech became thickened and drawling. The disease pursued a steady, progressive course, and, while the bodily nutrition was well maintained, the involuntary movements were more intense, and about eighteen months later mental symptoms became apparent. He subsequently applied for admission to the National Soldiers' Home, and was admitted May 15, 1909. While at the Soldiers' Home he became very untidy and slovenly, and exceedingly inadvertent in his habits. He was captious, unreasonable, had outbursts of hyperirritability, and finally displayed such distinct symptoms of mental deterioration that he was transferred to the Government Hospital for Insane in August, 1909.

Condition on Admission.—The patient was a medium-sized, fairly well-nourished man. His height was 5 feet 7 inches, weight 126 pounds. The skin and cutaneous membranes were normal. No stigmata of degeneration could be detected. Examination of the respiratory system showed no signs of pulmonary disease. The great pectoral muscles were occasionally jerked violently, but this did not embarrass the respiratory movements. Pulmonary sounds were normal, and the heart outlines within normal

limits. The peripheral vessels showed no evidence of sclerosis. The genitourinary system was normal. Temperature and pulse normal. Urinalysis negative.

Neurological Examination.—Cranial nerves: The pupils were equal, regular, medium in size, and reacted normally to accommodation and light, directly and consensually. Vision was normal. No involuntary ocular movements were apparent. There was no nystagmus. The corneal reflexes were active and the facial sensibility was not defective. The facial expression was modified by slow, involuntary muscular contractions. No dysphagia was evident. The palatal reflex was normal. Taste, smell and hearing were normal.

Speech was thickened and drawling, the enunciation indistinct and many words went together with a slurring effect.

Sensory System.—Tactile sense showed no deviation from the normal. Pain sense normal. He readily recognized marked variations in temperature, but finer changes with difficulty. The muscle sense was intact. Stereognostic sense not impaired.

Reflexes.—The arm jerk was equally brisk in both arms. Wrist jerk sharp. Knee jerks were markedly exaggerated. Tendo-achilles were present and equal. There was no clonus. Both the right and left plantar responses were flexor. Cremasteric, epigastric and abdominal reflexes were somewhat hyperactive. The function of the organic sphincters was not disturbed.

Motor System.—The musculature, especially of his extremities, was firm and well developed from constant, though involuntary, use. No fibrillation could be detected and contractures were absent. The case presented the characteristic involuntary choreiform movements. During the waking hours they were never absent, but subsided during sleep. With excitement or exertion they became more violent. The muscles of his extremities and head jerk irregularly, and when he attempted to arise from the sitting position his legs were thrown forward with an excessive amount of movement, and in consequence he had difficulty in gaining his equilibrium. A similar exaggeration of his usual involuntary motions occurred when arising from the prone position, and his arms and legs swung about in an aimless manner. When standing his body swayed considerably. In walking his head was generally inclined forward; his steps were about the usual length, but uncertain, owing to the jerky movements, and one leg was frequently thrown in front of the other, causing the gait to closely resemble that of drunkenness. The movements were of about equal intensity in the muscle groups of the legs, arms, head and face. The movements of the facial muscles frequently produced strange contortions and grimaces. The head was jerked forward, backward and laterally, and the resulting peculiar gestures, poses and exaggerations of action were prominent. Movements of the muscles of the trunk also occurred, especially of the abdominal group. He was able by strong effort to somewhat inhibit these movements for a brief period, but this temporary inhibition was invariably followed by a period during which the move-

ments were excessive. There was no evidence of fatigue as a result of the continuous muscular action.

Mental Condition.—A general mental deterioration of a slow, progressive character occurred. He was usually inclined to be somewhat retiring and content, although he frequently asked for a parole or permission to return to the Soldiers' Home. His personal habits were slovenly and he required close supervision, owing to his general neglect and inadvertence. A narrowing of the mental horizon and interest and a lack of insight into his condition were perceptible. Occasionally he displayed considerable irritability, at which times he would assault other patients.

There was some evidence of hallucinations and delusions in the early stage of the disease, which, however, were not prominent and faded as the dementia progressed.

Orientation was imperfect. General memory fair, but specific memory for recent and remote events was quite poor.

The physical deterioration of the patient became quite pronounced during the last three months of his life. On the evening of March 25 his temperature rose to 102, and râles could be heard in various parts of the chest. On March 28 areas of dullness were perceptible. The temperature fluctuated between 101° and 103°, and the patient died on April 1, 1913, after a duration of the disease for about eight years.

SUMMARY OF THE CLINICAL HISTORY.—A young man 25 years of age, in whose family no hereditary factors could be discovered; whose mental and physical development was up to the normal standard, and who had never had any particular illness, other than tropical dysentery, suffered with symptoms of nervousness in the spring of 1905. In the course of a few months considerable alteration in his general condition occurred. Involuntary choreiform muscular movements developed, first affecting his upper extremities, causing his fingers to move and his hands to start. Shortly after his legs became affected. The involuntary movements of his legs caused his gait to assume a markedly swaying character. Upon consulting a neurologist he was apprised of the true nature of his ailment.

The symptoms steadily progressed; a few months later the muscles of his face became involved, and at the same time articulation became somewhat defective. The involuntary movements became more intense and in about eighteen months disturbance of the intellect was perceptible.

He was admitted to the Soldiers' Home in May, 1909, and while there displayed hyperirritability, became untidy in his habits, and was transferred to the Government Hospital for the Insane in August, 1909.

Examination showed that the pupil reflexes were normal; vision was normal; there was no nystagmus; pain sense was normal; slight variations in temperature were not readily appreciated. Muscle and stereognostic sense normal; tendon reflexes were exaggerated; no ankle clonus or sphincter impairment. It is therefore apparent that the usual signs of organic disease of the pyramidal system were absent, but the involuntary muscular movements indicated a profound disturbance of motility.

The course of the disease was marked by an increase in the motor symptoms and a general mental and physical deterioration of a slow, progressive character. He died on April 1, 1913, from bronchopneumonia.

AUTOPSY.—*External Examination.*—Body: Medium sized and emaciated. Slight post mortem lividity was present.

Internal Examination.—Head: The calvarium was symmetrical, wall thick, diploe compact. Dura slightly thickened, but neither adherent nor discolored. Inner surface smooth. Pia stripped readily and appeared normal. The subarachnoid spaces were not distended, and the cerebrospinal fluid was not increased.

Brain: Weight, 1290 gm. The cerebral hemispheres were well developed and showed no visible atrophy or widening of the fissures. The arteries at the base presented no perceptible abnormality. The spinal cord macroscopically appeared to be normal. Transverse sections at different levels were of good size, and no evidence of degeneration was discernible. The membranes showed no turbidity or thickening. The brain and spinal cord, together with portions of peripheral nerves, were placed in 10 per cent formalin for preliminary hardening.

Thorax: Pericardium normal. Heart, weight, 230 gm. Right auricle normal. Tricuspid orifice admits four fingers; valve normal. Right ventricular wall thinned. Pulmonary valve normal. Left auricle enlarged; mitral orifice admits two fingers; valve thickened. Left ventricular wall somewhat thinned. Aortic leaflets slightly thickened.

Lungs: Weight, right, 790 gm; left, 730 gm. Congested and contained consolidated areas in lower lobes.

Abdomen: Liver, weight, 1230 gm. Surface smooth, capsule somewhat thickened. Passive congestion. Gall bladder normal. Spleen, weight, 110 gm. Capsule thickened; surface smooth; pulp

soft and red in color. Pancreas, stomach and intestines normal.

Genitourinary Tract: Kidneys, weight, right, 120 gm.; left 150 gm. Right kidney surface smooth; capsule strips readily; cortex slightly thickened and well defined. Left kidney same condition. Bladder, mucous membrane congested.

The suprarenal bodies, pituitary and thymus glands were removed and examined, but presented no deviation from the normal.

Microscopical Study.

After hardening in formal, the central parts of the cerebral hemispheres, including the basal ganglia, were cut into a series of thin slices, the left by vertical and the right by horizontal incisions. Some of these were utilized for different tissue stains, while others were placed in Muller's solution for the Weigert method.

On the right side, however, the central part of the hemisphere was examined in almost serial sections by Weigert's stain.

Numerous pieces were also taken from various regions of the brain for microscopical study, together with portions of the spinal cord and peripheral nerves.

The following histological methods were employed: Thionin, Nissl, toluidin blue, cresyl violet, Van Gieson, hæmatoxylin-eosin, polychrome methylene blue, Mallory, Mann, gentian violet, Weigert's resorcin-fuchsin, Herxheimer, Soudan III, Bielschowsky, Alzheimer's for glia, Weigert's for neuroglia fibers, Marchi, Spielmeyer, Weigert-Pal, Weigert's myelin-sheath and others.

Meninges.—The pia-arachnoid showed a very slight thickening, but no infiltration or other pathological changes could be found.

Brain.—A study of numerous sections from the precentral gyre revealed some very interesting and important facts. The most striking feature, from a cytological aspect, was the remarkable preservation of the giant cells of Betz. These cells, for the most part, were not altered in staining reaction or morphological characteristics. A few of them only showed beginning pigmentary degeneration with some tigrolysis Pathological changes of varying degrees of severity were discernible, however, in many of the neurons other than Betz cells, but especially in the deeper layers of the cortex. A more or less extensive deficiency of the chromophilous substance was visible in the degenerated ganglion cells.

In those neurons which showed total tigrolysis a row of small irregular-shaped granules, representing the remains of disintegrated Nissl corpuscles, usually defined the periphery of the cell bodies. In some instances the disintegration was of such a character that the chromophilic substance appeared as a fine powder, while occasionally cells were seen which had lost all their tigroid bodies. Such cells were often reduced to mere shadows. Sometimes the disintegrated granules occurred in groups, and here and there large irregular masses were seen distributed in the cell bodies. Not infrequently ganglion cells were observed in which the Nissl corpuscles presented a normal disposition within the cell bodies, but within the dendritic processes an extremely fine granular disintegration was visible. It was apparent that these changes represented different degrees of the same regressive process.

The nuclei also showed some interesting deviations from the normal. The nucleus was frequently dislocated and occupied an eccentric position near the periphery of the cells. The nuclear membrane was usually distinct, but the contour of the nucleus irregular. Folding of the nuclear membrane sometimes occurred. The nucleus of some cells stained deeply with toluidin blue, but in other instances were swollen, stained lightly and the outline of the nuclear membrane was almost indistinguishable. The lipoid substance in many cells appeared to be abnormally increased, and in a few of them an advanced stage of pigmentary degeneration was discernible. This material appeared as irregular-shaped masses of a yellowish tinge lying within the violet-colored cytoplasm.

The most frequent alteration encountered in those cells which showed degenerative changes was characterized by a general shrinkage of the achromatic substance. The chromophilitic bodies within the cytoplasm and dendritic processes appeared to be more darkly stained. In a few instances the shrinkage was quite excessive, and in consequence the cells presented a rather elongated appearance. The nuclei in most of these cells were centrally situated and no marked pathological changes could be detected. When stained with the Bielschowsky method for neurofibrils these elements were usually seen to be continuous through the body and processes. The functional activity of such cells was obviously impaired, but there was no reason to assume that it was entirely lost.

Some cells were swollen and the chromatic substance faintly stained. The nuclei were enlarged, pale and of an irregular contour. The nucleoli were likewise distended, and stained metachromatically. The nuclear membrane was ofttimes scarcely discernible and the nucleoplasm presented a stippled aspect. The cytoplasm appeared to have undergone a fine granular disintegration, and the dendritic processes and axis cylinder were traceable for only a limited distance. A few ganglion cells were evident which were distinguished by the intense dark staining of the cell bodies and process. The apical processes were unusually tortuous and could be traced for a considerable distance. The neuraxis process was shrunken. The nuclei were sometimes eccentrically located and the nucleoli increased in size. These cells were deeply stained by the Bielschowsky method. The nuclei were angular and of a dark-brown color. In some, groups of small granules were seen lying within the nucleus.

Concomitant with these alterations of the nerve cells, pathological changes in the neuroglia tissue were evident. These were distinguished by both progressive and regressive changes, an increase of neurolgia cells and a hyperplasia of glia fibers were discernible, chiefly confined to the lower layers of the cortex, where the degeneration of the ganglion cells was greatest. A marked proliferation of small astrocyte cells having densely stained nuclei, and more or less erratic-shaped darkly colored cell bodies, was in evidence, and formed the most distinctive feature of the gliagenetic process. Sometimes the nuclei of the glia cells were distorted, and presented an angular, shrunken, darkly stained homogeneous aspect. The cytoplasm in some instances contained cystic-like masses of lipoid substance, which usually stained a yellowish green color. Similar masses of fatty material were occasionally seen in the protoplasmic processes.

Neuroglia cells were also encountered with enlarged, lightly stained nuclei. The nuclear membrane appeared somewhat attenuated. Within the nucleoplasm several metachromatically stained nucleoli were usually discernible, lying within the delicate net-like structure joining the blue stained chromatin particles. The protoplasm was as a rule abundant, more or less ill-defined, faintly stained, and not infrequently contained lipoid granules.

A satellitosis was readily perceptible in the vicinity of ganglion

cells, and gliogenous cells were occasionally seen within the cytoplasm and processes of degenerated nerve cells.

With Weigert's method for neuroglia a considerable increase in glia fibers was perceptible in the lower layers of the cortex. The membrana glia superficialis appeared normal. The fibers of the cortex were investigated by the Weigert-Pal and Bielschowsky methods. The tangential fibers were in general slightly diminished and in some areas appeared to be extremely reduced. The fibers forming the interradiary and superradiary plexus were likewise somewhat defective.

The majority of the vessels were unaltered and showed no perceptible thickening of their walls or enlargement of the Virchow-Robin space. In the layers of the cortex, however, where cellular degeneration was in evidence, the adventitial spaces of many vessels were dilated, and, as a rule, filled with Körnchen cells and irregular shaped masses of greenish-colored lipoid pigment. The nuclei of the adventitial cells were frequently shrunken, stained darkly and their cytoplasm contained granules of lipoid and basophilic metachromatic substance. Yellowish colored granules were also occasionally discernible in the cells of the muscular coat.

The pathological alterations in the postcentral and paracentral convolution were quite similar to those found in the precentral gyre, both in regard to the cellular changes and the fiber content.

An examination of sections from the gyre of the frontal lobe showed diverse alterations in the shape, size and staining reaction of some of the nerve cells throughout the cortex in this region. A few of the cells appeared swollen and faintly stained. In others chromatolytic changes were in evidence. A marked change in the distribution of the tigroid bodies was discernible, and instead of the usual appearance, fine granules were seen arranged in groups or irregularly scattered through the cell. Some of the cells showed a considerable increase of lipoid pigment. A number of cells were encountered which appeared shrunken. Eccentricity of the nucleus sometimes occurred. In the markedly altered cells the nucleus was sometimes shrunken and difficult to distinguish from the protoplasm of the cell, owing to the fact that it stained uniformly throughout. A disintegration of the neurofibrils was visible in some instances by the Bielschowsky method, and the tangential fibers were more scanty than usual. The pathological

changes affecting the glia cells resembled those described in the precentral region. Proliferation of the neuroglia cells occurred mostly in the lower layers of the cortex. The nuclei appeared shrunken, excessively stained and frequently presented a homogeneous aspect. Glia cells were occasionally encountered in the vicinity of degenerated ganglion cells, having rod-like nuclei. Regressive changes were present, and accumulations of pigment were discernible within the protoplasm.

The adventitial spaces of some of the vessels were distended and contained products of disintegration, but otherwise appeared unimpaired.

The cellular alterations in the cortex of the insular region, the temporal and occipital lobes, were analogous to those found in the frontal gyri, but somewhat less extensive.

In the hippocampal region some of the pyramidal cells were shrunken, elongated and deeply stained. No marked proliferation of the glia was present, or pathological alterations of the vessels.

Basal Ganglia.—In the optic thalamus circumscribed groups of ganglion cells were encountered which presented a striking appearance, owing to their pale staining in contrast to the surrounding cells. Many of the ganglion cells showed intense pathological changes. In some of the cells the chromatin granules appeared as a fine dust in the center of the cytoplasm and in the vicinity of the nucleus, while at the borders the granules were larger and more darkly stained. Most of these cells had become round in form and their processes showed changes similar to those occurring in the cell body. The nucleus was, in many instances, pressed to the periphery of the cells, stained more darkly than usual, and was sometimes difficult to distinguish from the cytoplasm. Some cells were swollen and the chromophilic bodies appeared as a lightly stained fine dust; the processes were likewise palely stained. Although the nuclei of these cells were distorted and eccentric, the nuclear membrane remained intact. Regressive changes in the nucleolus were frequently discernible. These alterations were readily distinguishable from those types of cellular degeneration in which nothing remained of the cell body other than a row of irregular shaped basophilic granules surrounding enlarged metachromatically stained nuclei whose nuclear membrane had disappeared. Sometimes the nuclei presented an elongated or oval form and

were more deeply stained than the granular masses; in other instances the centers of the nuclei had vanished.

Cells with a reticular arrangement of the chromatin and with more or less shrinkage of the nuclei were not infrequently encountered.

With the Bielschowsky method the neurofibrils in many cells were seen to be discontinuous and appeared as fine granules. Increase in the neuroglia tissue was quite evident. Glia cells having two or three nuclei were often encountered, and areas were present where the neuroglia elements grouped together in large numbers.

Satellitosis was marked and glia elements were frequently seen within the cytoplasm of ganglion cells. Some of these parasitical-like glia cells showed regressive changes, but in general progressive changes were prominent. No lipoid substance was visible in some of the neuroglia elements in the vicinity of degenerated ganglion cells.

In certain parts circumscribed areas were intensely diseased, whereas the immediately surrounding region appeared almost normal. Such areas of degeneration could be observed to a greater or less extent around some of the vessels, which themselves appeared but slightly affected.

The adventitial spaces of most vessels traversing degenerated areas were enlarged and to a greater or less extent filled with disintegration products. This substance occurred in the form of yellowish pigment, staining with different degrees of intensity with basic aniline dyes. Lying within these masses a nucleus was frequently visible, which usually presented a pycnotic condition; a progressive vacuolar degeneration; or, in other instances, a polyhedral or triangular shape, characterizing it as the nucleus of a Körnchen cell. Ofttimes, in consequence of the compactness and intense staining of the granules, no nucleus was discernible in such accumulations. With the Herxheimer method the greater quantity of this material could be distinguishable as lipoid substances within the cytoplasm of Körnchen cells. However, large aggregations of a fatty character were discernible lying free within the lymph spaces. It was interesting to observe that such lumps usually presented a regular, roundish contour, but when closely packed together were exceedingly irregular in form, which

gave the impression that this substance may have been in a fluid or semi-fluid state before fixation.

In sections stained with toluidin blue some Körnchen cells were seen to contain basophilic metachromatic substances mingled with greenish tinged granules. Similar material was also perceived in neighboring glia cells. Many vessels and capillaries showed a considerable widening of the adventitial lymph spaces, which contained neither products of disintegration nor infiltrating elements.

The adventitial coat of some of the arteries was slightly thickened, but no trace of endarteritis could be perceived in any of them, and not a single obliterated vessel was encountered. Although these pathological changes were perceptible in the different nuclei of the thalamus, the nerve cells of the lateral nucleus appeared more intensely affected.

Examination of the lenticulate nucleus showed it to be similarly diseased.

With the Nissl method it was apparent that an unusually high grade degeneration of the ganglion cells was present in this region. Hardly a single cell could be found which did not exhibit marked pathological changes. In many of the diseased cells the changes in the nuclei were striking; vacuoles were discernible in the cell body, and the chromophilic substance was irregularly disposed in lumps or fine granules within the cytoplasm and processes. Numerous cells appeared as mere shadows surrounded by faintly colored granules. A pronounced increase in the cell pigment was a prominent feature of the degenerative changes in some instances; other cells were shrunken and sclerotic. The neuroglia tissue was greatly increased.

The cytoplasm of the glia cells lying between the nerve elements had undergone an almost incredible hyperplasia, with nuclear proliferation of a progressive character.

Regressive changes of the glia were also seen, frequently appearing as small nuclei lying within an enlarged cell body. A pronounced gliosis occurred in the vicinity of many capillaries.

Circumscribed foci of degeneration analogous to those found in the thalamus were encountered. In the degenerated areas many Körnchen cells were in evidence, their cytoplasm in most cases filled with yellowish, or yellowish-green, colored granules. Gliogenous phagocytic cells not infrequently occurred in groups, espe-

cially around capillaries, passing through or in the neighborhood of degenerated areas. Where many of these cells were collected about a blood vessel the enlarged perivascular spaces were seen to contain small and large irregular shaped masses of a yellowish tinge, and much peculiar material representing in part at least coagulation products of pathological tissue fluids. Apparently the cells extruded substances into the same space.

In these areas lipoid granules were visible in the cytoplasm of the cellular elements of the vessel walls, especially of the adventitial lymph space.

No trace of endarteritis could be perceived in any of the vessels. Neither obliteration of capillaries, hemorrhages, proliferation of the vascular endothelium nor any evidence of sprouting new capillaries could be found.

A careful investigation of the fiber content of the basal ganglia, internal capsule and subthalamic region was made by the Weigert and Weigert-Pal methods.

In sections through the upper part of the right corpus striatum, the fine fibers passing mesially from the putamen were unaffected. The fibers of the internal capsule also appeared unaltered.

At a somewhat lower level, however, the internuncial fibers were diminished, and the medullary laminæ were defective, and atrophy of the nucleus was quite apparent. The external capsule presented a normal appearance. In the lower part of the nucleus the atrophy was more pronounced, the external and internal laminæ were considerably degenerated, the internuncial fibers were atrophic and some of them had disappeared. The internal capsule stained normally in all the sections and no degenerated fibers could be detected.

The slender tracts of fibers passing through the capsule and uniting the caudate and lenticulate nuclei were somewhat reduced in number, but most of them appeared normal.

Relative to the fibers of the optic thalamus a considerable diminution could be observed in the vicinity of the lateral nucleus, and a reduction in the fibers of the external medullary lamina was likewise visible. A number of the striothalamic fibers were degenerated.

In the subthalamic region it was evident that some of the nerve fibers of the zona incerta had undergone degeneration. Many of

the fibers of the lenticular loop in its course around the medio-ventral border of the basis pedunculi were degenerated. A number of the fibers of that portion of this tract which passes to the corpus Luysii were also affected. A deficiency in the fibers of the fasciculus retroflexus was apparent. The subthalamic nucleus was somewhat atrophic, but the majority of its fibers were fairly well preserved. The field of Forel appeared somewhat altered.

Crura Cerebri.—No defects in the crusta were visible in sections stained by the Weigert-Pal method. The fibers of the pyramidal tract stained deeply, and were not diminished in quantity. The mesial and lateral sectors were unaffected.

The tegmentum was apparently normal, but some of the cells of the substantia nigra were slightly altered. The fiber content of the nucleus ruber was impaired. A considerable number of the nerve cells were affected. In many of them various stages of chromatolysis was visible; others showed pronounced pigmentary degeneration.

Some of the cells were shrunken and their apical processes more tortuous than usual. Marked increase in the neuroglia elements was obvious, and proliferative changes in evidence. A gliosis occurred around many of the nerve cells which were intensely degenerated; and not infrequently only a few remnants of the cytoplasm were still discernible.

Medulla Oblongata and Pons.—No degeneration in the medullated fibers could be discovered by the Weigert method. The corticospinal tracts stained normally and no atrophy or loss of fibers was apparent. The fillet, olives, and restiform bodies also appeared normal. No characteristic degenerations could be found by the Marchi method. The cells of the motor cranial nuclei, with the exception of a few showed no appreciable deviation from the normal. Some of them were slightly shrunken, stained darkly and their processes appeared unusually wavy. In others a granular degeneration of the neurofibrils was perceptible. Similar changes occurred in a few of the cells of the nucleus cuneatus and nucleus gracilis. There were no changes in the pons that could be regarded as pathological.

Cerebellum.—A few of the Purkinje cells show chromatolytic changes, and neurofibrillar disintegration was visible in some cells.

The granular layer presented no departure from the normal, but a slight increase of glia cells was apparent in the molecular layer. No fiber decrease could be detected with the Bielschowsky or Weigert-Pal methods. A few of the cells in the corpus dentatum were shrunken and atrophic; but in general no changes were detected in the large triangular and stellate cells of this nucleus which could be regarded as pathological. No appreciable defect was discoverable in its rich plexus of nerve fibers.

Spinal Cord.—Slight diffuse connective tissue-thickening of the pia was present, but cellular infiltration was entirely absent, and no evidence of any inflammatory process could be discovered. The spinal vessels appeared normal; no thickening of their walls or endarteritic changes were discernible.

The cells were carefully examined in the cervical, dorsal and lumbar regions of the cord.

In the cervical region the motor cells of the anterior horns were well preserved. The majority were of good shape, the chromophilic bodies well defined and the nuclei centrally located. In these cells no abnormal increase in pigment or other pathological changes were visible. Some of the cells, however, were shrunken, stained more deeply than usual, and the typical arrangement of the Nissl elements disturbed. In the posterior horns it was also evident that some of the cells had undergone certain pathological changes, consisting in a slight shrinkage of the hyaloplasm, causing a more compact arrangement of the tigroid bodies, and in consequence a deeper-stained appearance to the cell. Such cells often had an elongated aspect and tortuous processes. The nucleus stained darkly, but otherwise appeared unaltered. A few of the cells of the lateral horns were slightly swollen and commencing chromatolysis was visible round the nuclei. The motor cells of the anterior horns in the dorsal region showed no distinctive alteration. In some of the cells of the posterior horns, however, a granular disintegration of the tigroid bodies occurred; others showed some pigmentary degeneration. In the lumbar region the cells of the anterior horns were well preserved. Here and there a cell was encountered in which the characteristic arrangement of the Nissl substance was affected, but otherwise no alteration could be detected. Pigmentary degeneration was discernible in a few of

the cells of the posterior horns; in others commencing chromatolysis was perceptible.

Longitudinal and cross sections were made from different levels of the cord for the investigation of the fibers.

The sections stained by Weigert's method were negative, and there was no indication of degeneration or shrinkage in any of the columns of the cord.

The direct and crossed pyramidal tracts showed no change. The medullated fibers of the gray matter appeared normal. With Marchi's method the picture was likewise negative. No evidence of systematized fiber degeneration was apparent in the cortico-spinal tracts in any part of the cord. A few typically degenerated fibers were encountered in longitudinal sections by the Alzheimer-Mann method.

Peripheral Nerves.—Sections from the ulnaris, radialis, medianus and ischiadicus were carefully examined, but failed to disclose any pathological alterations.

Résumé of the Anatomical Findings.

The brain was firm, large and well developed. There was no evidence of atrophy, and the convolutions presented a normal disposition. The meninges were normal, other than an inconsiderable thickening of the pia-arachnoid in some places. The cerebral vessels showed no deviation from the normal. The lateral ventricles were not dilated and no ependymitis was present.

Microscopically, the pathological changes in the cortex of the brain were distinguished by alterations in the nerve cells and neuroglia tissue. These changes were approximately uniform in the cortex of the different lobes, but apparently most pronounced in the frontal region. The alterations in the ganglion cells were confined chiefly to the small and medium-sized pyramids, and were characterized principally by shrinkage, although various types of cell disease were in evidence.

In the motor region the giant cells of Betz were exceptionally well preserved.

The neuroglia tissue showed both progressive and regressive changes. A considerable increase in the number of small astrocytic cells was present. Deficiency of the tangential fibers was discernible in some areas. The white matter of the cerebral hemi-

spheres was normal; and the pyramidal system, traced from its origin in the Betz cells of the motor area throughout its course, presented no alterations of any significance.

In the optic thalamus intense degeneration of the nerve cells, with an enormous increase of the neuroglia tissue, was found in the external nucleus, but small circumscribed areas of degeneration were also discernible scattered through the ganglia. The lenticulate nucleus was similarly affected, but the degeneration appeared more diffuse. Many of the nerve cells had vanished, and a marked neuroglial hyperplasia was present. The changes in the caudate nucleus were less severe.

The vessels of the diseased areas showed an enlargement of their adventitial spaces, and in some instances slight thickening, but were otherwise unaltered.

The internal capsule was intact, but the striothalamic fibers were reduced. Some of the fibers of the lenticular loop were degenerated, and the subthalamic nucleus appeared somewhat atrophic. The fasciculus retroflexus Meynert was slightly affected. A number of the cells of the tegmental nucleus were considerably altered, and increase of the glia cells was perceptible.

No systematized fiber degeneration could be found in the spinal cord, and the motor cells of the anterior horns, with the exception of a few, presented a normal appearance.

The interesting features in this case are the early onset of the disease, the absence of homogeneous heredity, and the pathological changes.

Huntington, who was the first to give a full description of this disease, referred to its independence and differentiation from other types of chorea, especially Sydenham's chorea.

He laid especial emphasis upon heredity as a salient etiological factor, and the development of the disease late in adult life. While in general the disease does not usually occur until the third or fourth decade, it is obvious, from a review of the literature, that the affection may become apparent at a much earlier period in life. Menzies and others have observed that the age at which it appears frequently precesses generation by generation, but the exceptions are numerous. Heilbronner has suggested that the earlier manifestations of the affliction may correspond to a severer course of the disease.

An instance in which the disease began unusually early in life has been described by Friedenthal. Hoffmann demonstrated a case in which the first symptoms of the disease were exhibited in the twentieth year of the patient's life. Diller mentions 10 cases which developed before the twenty-fifth year; and Kölpin reported a case beginning in the twenty-second year. In a case published by Goldstein, the choreic movements became evident between the twenty-second and twenty-third years of age. Wollenberg also reported a case in which the disease began at the age of twenty, terminating in dementia. A number of other cases occurring quite early in life have been published.

Chronic progressive chorea is probably one of the most familial of all diseases, and heredity has been regarded as a significant etiological factor.

In the case under consideration the absence of hereditary transmission and degenerative stigmata is striking.

Among some instances in which no heredity could be ascertained may be cited the case reported by Frank. The patient was affected with the disease in her forty-third year; the choreic movements began in her right arm and gradually involved the entire body. The mental symptoms were characterized by irritability and a progressive deterioration of the intellect. Schabad describes a case which developed in a woman forty years of age, who had suffered for a number of years with attacks of migraine. No hereditary factors could be determined. Continuous movement of the head and unrest of the musculature occurred; extensive involuntary movements of the upper extremities and constant extension and contractions of the lower extremities were present. Excitement increased the symptoms. The movements could be influenced to a slight degree by the will, and practically ceased during sleep. Speech was affected and mental reduction evident.

In one of two cases reported by Westphal the cause of the disease was attributed to injuries sustained by the patient in falling from a scaffold. Shortly after his discharge from the hospital choreic movements developed, which subsequently increased in intensity. Speech was affected, the reflexes exaggerated and an apathetic progressive dementia supervened. In one of three cases described by Frotscher no heredity could be determined. The patient was struck on the head by a heavy beam and subsequently

developed chronic progressive chorea. Skoczynski reports the case of a woman who developed chronic progressive chorea following a severe fright, caused by a fire in the patient's house. No hereditary factors could be ascertained. A. de Castro, Bonfigli, and others have also reported cases in which hereditary factors were wanting.

In considering the morbid anatomy of chronic progressive chorea it is apparent, upon reviewing the literature, that many of the pathological observations recorded afford but meager data toward an explanation of its semeiological characteristics.

The unsatisfactory results are in part due to the fact that early cases seldom die and advanced ones are to a greater or lesser degree complicated by pathological tissue changes quite sufficient to conceal the slight morbid impairment presumably responsible for the symptoms, thus causing a lack of uniformity and a variation in the descriptions of the pathological alterations.

It therefore appears evident that chronic pachy- and leptomeningitis, hydrocephalus, œdema, and vascular changes assumed by some authors (Oppenheim, Facklam, Weidenhammer, Wollenberg), as the pathological basis of the disease, can hardly be accepted as enacting more than a casual rôle in its morbid anatomy, as similar conditions are not uncommonly observed at autopsy in arteriosclerotic and senile types of dementia, with which advanced cases of chronic progressive chorea are frequently associated. Hence cases of this description are obviously unsuitable for pathological investigation. It is therefore probable that in consequence of such terminal complications some of the earlier authors (Weidenhammer-Binswanger), at a time when the histological processes in paresis and senile dementia were obscure, believed that an analogy existed between these diseases and chronic progressive chorea. There are, however, at present a number of cases on record in which the pathological alterations observed could in no way be confounded with those produced by a syphilitic process. Likewise in our case there was no pathological lesion of the vessels, or meninges, which resembled what is found in syphilitic diseases of these structures, and the Wassermann test obtained during life proved negative. In view of these facts, there is no reason why syphilis should be advanced as a possible basis for this disease.

A frequent microscopical change observed by writers on this subject is a hyperplasia of the glia in the cortex of the cerebrum. This increase of neuroglia has been described either as a uniform process throughout the cortex, or more pronounced in certain layers, and varying considerably in its degree of intensity. Some investigators have reported a general increase of glia cells (Greppin, Modena, et al.). Clarke found the neuroglia increased in the second and third layers of the cortex. Collins reports a hyperplasia of glia chiefly in the deeper layers; Schulz an increase in the number of neuroglia cells in the layer of large pyramids; Menzies a coarseness of neuroglia in the first layer. Raecke found the glial increase most marked in the motor region. Stier describes a proliferation of glia cells principally in the layer of small and medium-sized pyramids, which he regards as a primary process resulting from an inherited anomaly of the cortex. A number of writers have therefore concluded that a hyperplasia of the glia constitutes the characteristic alteration in Huntington's chorea.

Lannois and Paviot proposed an explanation for the involuntary movements occurring in this disease, by the hypothesis that an irritation of the otherwise intact giant cells is produced by the proliferating glia, thus inciting them to excessive function. Keraval and Raviart, Kattwinkel, and more recently Margulies, have advanced similar theories. This hypothesis, however, seems most improbable, as it is difficult to conceive how an irritative reaction of the glia could continue for years, and the motor cells retain their integrity.

It appears obvious that undue prominence has been given by some investigators to the increase of the glia, as a factor in the pathogenesis of this disease. A careful review of the more important contributions to the pathology of chronic progressive chorea, together with the observations here reported, indicate that the hyperplasia of glia occurring in this condition can in no sense be considered a primary process, as opined by Stier, but that the changes in the neuroglia are secondary or reparatory in character, consequent upon degeneration of the neuronic elements.

Structural anomaly in the architectonic of the cortex has been suggested by Kölpin as a possible foundation for the development of the disease. But this offers no adequate explanation for the

usual late manifestation of the symptoms and the progressive character of the affliction.

A diffuse degeneration of the ganglion cells of the cortex is the most constant pathological alteration which has been described in this disease. In some instances the nerve cells in certain layers were more intensely affected. Menzies found the degeneration of the cells most pronounced in the deeper layers; Rusk, Stier, and others the greatest variation in the small and medium-sized pyramids. The failure of most investigators to find any alterations in the Betz cells which could be regarded as pathological is significant (Greppin, Stier, Rusk, Kölpin, Raecke, Pfeiffer). Other writers have observed a variable amount of disease in the cellular elements of the cortex and basal ganglia (Modena, Margulies, Alzheimer).

In this connection it is interesting to note that the severity in the alterations of the nerve cells and the extent of defectiveness in the cortical fibers, seem to vary in proportion to the degree of dementia.

A slight marginal loss, or irregular degeneration, in a few fibers of the spinal cord has been observed, but such changes may occur normally, especially in aged individuals.

From the exhaustive anatomical study in the case here reported, we may conclude that the involuntary movements in this disease probably result from a primary degeneration of the neurons in the nucleus ruber, the lateral nucleus of the optic thalamus and the lenticulate nucleus, thus interfering with the conductive integrity of the cerebello-thalamo-rubro-cortical path.

As regards the brain and spinal cord, the motor cells were well preserved, and the cellular changes present were of a character similar to those encountered in conditions unassociated with choreiform movements. The pyramidal system was intact and no systematized fiber degeneration could be detected in the spinal cord.

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