MYATONIA CONGENITA: A REPORT OF A CASE WITH AUTOPSY *

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BOSTON

Oppenheim¹ described in 1900 a remarkable disease in children the chief symptom in which is a hypotonia or even atonia of the muscles, combined with a corresponding diminution of the tendon reflexes. There is limitation of active movement varying in degree. In the most marked cases the extremities lie motionless and apparently paralyzed. On close observation contractions may be brought out in some or many of the muscles, but these are weak and without locomotor effect. In one of his cases the affection involved not only the muscles of the extremities, but those of the neck and trunk also. The condition is always more marked in the lower than in the upper extremities and the muscles supplied by the cranial nerves are not affected. Electrical stimulation shows a quantitative diminution of contractility up to its complete disappearance. There is no reaction of degeneration and no loss of sensibility. The joints are abnormally movable owing to the flaccidity of the muscles. It is a congenital affection, but it does not usually attract attention immediately after birth. He considers that it consists essentially in a retarded development of the muscles, and it tends to betterment or recovery. He did not, however, exclude the possibility of an involvement of the nerves or of the anterior horn cells. The muscles may be flaccid and soft, but they are never atrophied.

CASE.—*History*.—M. G., aged 6 months. The father was addicted to alcohol and was intoxicated at the time of conception and at intervals during the mother's pregnancy. During pregnancy the mother was well, but much worried and distracted over her husband's condition. There have been no miscarriages. The child of a previous pregnancy is healthy. The previous history of the mother is negative. The child, male, was born normally April 3, 1910. Fetal movements were felt during pregnancy and were quite as lively as those of the normal baby of the previous pregnancy. When the baby was three weeks old, the mother noticed that he seemed unusually limp, but was re-assured by the obstetric nurse in charge. When six weeks old, the mother noticed a dropping of one hand and that the hands seemed weak and limp and were not moved as freely as they ought to be. At this time she consulted a physician who said the condition was due to weakness, that the breast milk was probably not agreeing with the baby and advised that it be taken off the breast. When the baby was two months old he was seen by Dr. Howland of New York who noted a marked atrophy of the muscles of the trunk and extremities, and deformity of the chest. The baby seemed to improve somewhat, at one time being able to move his arms, but later

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this power disappeared. He has never been able to move his legs at the hips, knees or ankles, but could make slight movements of the toes and fingers. He has never been able to sit up or to hold up the head. The mental development is normal. The breathing has been labored since the baby was three weeks old and this has grown progressively worse. On September 3 the baby caught cold and since then the trouble in breathing became worse, with choking spells from mucus accumulation. To give relief the adenoids were removed on September 24. The breathing was somewhat improved by the operation, but has lately become as bad as before. The weakness increased until he could no longer nurse from the breast or bottle and has to be fed with a spoon. The baby gained weight up to the time of the adenoid operation, but since then has lost.

Physical Examination.—October 3. Poorly developed and poorly nourished baby. The cranium was square, the forehead prominent; the fontanels depressed but of normal size; the mouth, tongue and throat were normal. There were no teeth. The pupils were equal and reacted normally. The respiration was irregular, labored and wholly diaphragmatic, but not notably accelerated. The chest showed marked increase in anteroposterior diameter. The heart, lungs, and abdomen were normal. The baby was entirely unable to hold up his head and there seemed to be a complete flaccid paralysis of the trapezius muscle. The upper extremities were not moved at all from the shoulder and very feebly at the elbow and wrist. The hands hung over in flexion when the arm was held upright. There appeared to be a flaccid paralysis of the shoulder girdle muscles with marked atrophy, particularly of the pectoralis. There was slight atrophy of the muscles of the extremities. The knee-jerk was absent.

From this time until death, October 23, the condition gradually became worse, although there were temporary ameliorations. There was increase in the mucus accumulations and in the fits of choking, and the child died in one of these attacks.

Autopsy.—The body was that of a somewhat emaciated, male infant; the body length corresponding to age; the weight below the average; no rash on surface of the body; all the tissues were very soft and flabby to the touch; no rigor mortis; all the joints were extremely flaccid and movable. The bones of the extremities were easily felt through the soft tissues; no edema; the skin was normal. The subcutaneous fat was small in amount, soft and somewhat edematous. The muscles of the neck were thin but of normal color and consistency. The pectoral muscles and all the muscles of the back and extremities greatly atrophied. The atrophy did not affect the abdominal muscles to so great a degree. The pectoralis major was reduced to a small fascia-like band. The color of the atrophied muscles was grayish and translucent. They were more succulent and the single muscles were not easily dissected out. They seemed infiltrated with fat and fused with the surrounding connective tissue. The intercostal muscles were reduced to thin gray sheets. The abdominal muscles, though thin, had a better color than the others. The large muscle masses alongside the vertebræ were reduced to thin bands less than 1 cm. in diameter. There seemed no change in the nerves. They were of normal size and appearance and more prominent than is usual. The thorax was misshapen. The antero-posterior diameter was greatly diminished; the cartilages and ribs passed almost backwards from the sternum, then took an accentuation of the normal curvature, giving a flat depression in the antero-lateral situation. The lower border of the thorax flared outward like the mouth of a bell. The diaphragm was of normal color, thickness and consistency. It seemed rather better developed than normal.

The tongue, pharynx, larynx, and trachea were normal; the tonsils and lymphoid tissue of the tongue and pharynx of a development corresponding to age. All the lymph-nodes of the body were prominent. The thyroid gland was small but of normal appearance. The thymus was large, of normal color and consistency. It projected 8 cm. below the sternal notch and weighed 29.2 gm. The heart weighed 36 gm., and in all respects was normal. The aorta and other

large vessels were normal with the exception of the left femoral, in which there was an occluding, fresh thrombus just below the origin of the profunda.

The entire upper lobe of the left lung and the upper posterior portion of the lower lobe were completely atelectatic and dark red in color. Nearly the entire upper lobe of the right lung was in same condition. There was no evident pneumonic consolidation, but all portions of the atelectatic lung sank in water. In the bronchi there was a small amount of muco-pus. The lower lobes of both lungs were normal; pleura normal; all the abdominal organs normal, as also were the brain and spinal cord on naked eye examination.

Diagnosis.—Anatomical diagnosis at autopsy, atrophy and degeneration of muscles, deformity of thorax, atelectasis of lungs, hypertrophy of thymus, fresh thrombus of femoral artery.

HISTOPATHOLOGY

The Muscles.—Portions of the various muscles were hardened in Zenker's fluid, liquor formaldehydi (formalin) and in Orth's fluid, sectioned in paraffin, and stained in methylene blue and eosin, in phosphotungstic hematoxylin and by the methods of Marchi and Weigert-Pal. All of the muscles affected showed the same changes though in a varying degree.

Cross section, hematoxylin and eosin: Section through some of the most altered muscles of the leg, with low power, shows the fibers arranged in well ordered fasciculi. The amount of connective tissue is increased. With low power, two well-defined masses of tissue can be seen. There are fibers which present the usual appearance of normal adult muscle. There are also masses of what seem to be accumulations of cells which are also arranged in fasciculi, but the masses are very much smaller than are the masses of normal muscles. Similar aggregations of cells are seen often at the periphery of a single muscle fasciculus. Occasionally, in the middle of the masses of small cells, single muscle fibers of the average size can be made out. At various places there are sections that appear to be the muscle spindles, that is, several muscle fibers enclosed in a definite capsule of connective tissue. The muscle fibers in the spindle vary greatly in size and the nuclei often show a central position.

Under the immersion, the larger fibers for the most part appear to be normal. Occasionally, the nuclei are found in the center of the fiber. What appeared under the low power as masses of small cells are seen to be composed of very small muscle fibers. Although most of these fine fibers are arranged in fasciculi, they are also found in the midst of the larger fibers and surrounding the groups of these. In the large fibers there is considerable variation in size, and they are usually round or oval. Many of the large fibers are vacuolated, containing either a single large vacuole, or several small ones. Some of these vacuoles contain a small amount of finely granular material. The largest fibers in this muscle are almost invariably definitely round. Occasionally, especially at the periphery of the muscular mass, fasciculi are found which seem to be midway between the larger muscle masses and the small fibers, but in general there is a sharp distinction between the two. With phosphotungstic hematoxylin there is a great variation in the muscle stain, some of the fibers being very much darker than others. The muscle fibrillæ are not well stained. In the fine fibers the fibrillæ are rather more prominent at the periphery of the fibers. On the longitudinal section of the muscles tissue, taken from about the same region, the same arrangement of the fibers can be distinguished. The cross and longitudinal striation is apparent in both sets of fibers, but more strongly marked in the larger fibers. The nuclei in the small muscle masses seem to be extremely numerous. They are of about the same size as in the larger fibers. Many of the fibrils are so small that when the section passes through a nucleus this occupies the whole extent of the fiber. The apparently great number of nuclei is due to the number of the fibers. When a single fiber is followed along, the nuclei are not more closely set than they are in the large fibers. The cross striations in a number of measurements are nearly the same distance apart in both the large and fine fibers. The length of the fine fibers could not be easily determined either by section or by teasing. They are

never so definitely parallel to one another as in the large fibers. The masses of the large fibrils in longitudinal section are perfectly straight; the masses of the smaller fibrils present a wavy appearance as though they had not contracted at the same rate as the larger fibers. Most of the small fibers are solid and they do not present the appearance of embryonic fibers. Occasionally, however, fibers are seen which are hollow with fibrillæ at the periphery presenting much the appearance of embryonic fibers, and a fiber solid throughout most of its course may present an area where it has hollowed out. They also occasionally present swellings along their course, but as a general thing they preserve the same diameter.

Size of the fibers.—Measurements were made of groups of the larger fibrils, taking those of both the largest and smallest diameter. The average diameter obtained by taking the longest and shortest diameters in a group of fifteen adjoining fibers is 19.2 microns. The largest fiber found in the interior of the group is 35 microns. The average diameter of another group of fibers is somewhat more, 23.75 microns. In a small group of 22 fibers, there is a variation in the sizes of the fibers which belonged to the class of large fibers of from 8 to 20 microns. The average diameter of a group of twenty-seven of the small fibers, only one diameter being necessary on account of the prevalent round shape, is 3 microns with a variation of from 1.5 to 3.5. In the longitudinal sections, fibers are found from 1.5 to 4 microns in diameter. On comparing the cross striations, taking two adjoining fibers of the large and small group, there is a difference in the distance between Krause's lines, this being from 1.8 microns to 2 microns in the large fiber and 2.4 microns in the small, this being evidently due to a difference in the degree of contraction. This difference did not always hold, but a number of careful measurements showed in other places slight differences in the distance between the lines. Here and there among the small fibers in the longitudinal sections, single fibers are seen which show neither longitudinal nor cross striation. In these fibers there are here and there sarcous elements in the shape of double dots and occasionally rows of a half dozen or more of such dots separated by the usual interval between Krause's lines. Comparison of these fibers with the fibers of the diaphragm show that the average of the diameter of the diaphragm fibers is the same as the large fibers in the affected muscle. A study of the muscle by the Marchi method shows changes more marked in the large fibers. There is no general fatty degeneration. Single very small fat drops were commonly present, and in certain fibers there was a large amount of fat. The largest amount of fat was found in the otherwise unaltered muscle of the diaphragm. In the small fibers it was exceptional that any fat whatever was found. A study of the connective tissue in the muscle showed that this was relatively increased, but it is uncertain whether there is an actual increase in this tissue. There is no evidence at any point of any active cellular changes in the muscle. There are no phagocytic cells and no foci of lymphoid cell infiltration. The blood vessels in the muscle are normal, but of small size. The vascularity seemed small, relative to the amount of tissue.

An attempt at comparison of the size of the muscles here with those of children of the same age led to nothing of importance owing to the extreme variation in the size of the muscles in varying conditions of nutrition. Thus in a greatly emaciated child of six months, the average size from the measurement of 112 fibers of the Sartorius muscle was 5.1 microns. Measurement of the palatal muscles of a well nourished infant at birth gave an average diameter of 17 microns; and the muscles of the larynx in a premature infant of seven months an average of 9 microns. We cannot definitely decide whether the size of the large fibers in this case varies from the normal, but probably it does not.

The nervous system.—Numerous sections made of the cortex, the cerebellum, the pons and medulla, and stained by the usual methods, showed in all respects a normal tissue. Sections of the cord at various levels, show very slight evidences of change. There seems no diminution in the number of cells in the anterior columns. The amount and distribution of the neuroglia is normal.

The Marchi stains show very slight degeneration of the myelin in the posterior columns. The degree, however, was so slight that in the routine examination of the cord it would probably have been unnoticed. The same applies to the anterior and posterior nerve roots, and to the spinal ganglia. In the Nissl stains of the cord, no certain evidence of cell degeneration can be made out. Sections were made of the sciatic nerve at various levels which were stained by the Marchi and Weigert methods and with hematoxylin and eosin. Here and there the sections stained by the Marchi and Weigert methods show very slight irregularity in the myelin. In single fibers there is a slight stain with the Marchi. There are no cellular changes in the nerve whatever. The examination of the nerves in the muscles show more marked changes. There are nerve bundles which are in all respects normal. The number of nerves, taking the whole mass of muscle, seems to be diminished, and among the fasciculi of small fibers, nerves are found which show evident degeneration and loss of myelin. A careful examination by the Weigert method leaves little doubt of the diminution of nerves in the changed muscle, that is, relative to the number of fibers. In these muscle fibers, no evidence is found of the terminal distribution of nerves to the single fibers. More or less definite nerve endings were found, however, among the fibers of normal size. Various branches of the sympathetic nerves which were found on the examination of the viscera, and branches of the pneumogastric nerves, were completely normal.

Sections of the atelectatic upper lobes of the lungs show congestion, atelectasis, edema, with small foci of bronchopneumonia. In the exudation here, a few diplococci conforming in morphology to pneumococci are found.

The myocardium is normal. An examination of the thrombus in the femoral artery shows this to have the usual composition of an acute thrombus, being made up of blood plates, fibrin, red corpuscles, and leukocytes. There was no examination of the blood made during life, but that within the vessels after death appears normal in the character and relative numbers of its cells.

The bone marrow of the femur shows a normal, active marrow.

It is very much regretted that there was no examination of the thymus. In the numerous pieces of tissue taken for examination, this was in some way lost. The numerous sections of the lymph-nodes show these to be normal with the exception of the almost complete absence of the germinal centers. The spleen is hyperemic, the follicles prominent, and in the germinal centers of these, almost without exception, there was extensive necrosis of a type exactly resembling that so commonly found in diphtheria. Microscopic examination of the liver, pancreas, adrenal, kidneys, intestinal canal and thyroid shows these organs to be normal. In the thyroid there is the usual amount of colloid.

ABSTRACTS OF CASES FROM THE LITERATURE

In view of the rarity and the interest of this disease, it seems worth while to give short abstracts of the cases hitherto reported.

MUGGIA.² Female child, family history negative. Pregnancy and birth normal. Directly after birth the child seemed normal. It cried, passed meconium, nursed and urinated. After a few days it was noticed that the child moved neither the arms nor legs. On observation, nutrition, size, weight and organs were normal. The limbs showed an absolute lax paralysis. The sensation of skin was normal. The superficial reflexes and the patellar reflexes were normal, but weakened. The electrical reaction of both nerves and muscles was not diminished. After four months' observation, there was no change in the condition and child continued to develop normally.

BATTEN.³ These three cases reported by Batten, the first case following Oppenheim's articles, are properly considered by Collier and Wilson to belong to the group:

CASE 1.—Male, age about 6 years; the third of four healthy children; never stood; could sit up but not kneel; was intelligent; on examination was thin and

small; could get into sitting position; progressed by rolling over and over; no localized atrophy or hypertrophy; all movements could be performed with arms; unable to extend legs or to flex legs on abdomen; extensors and flexors of foot were fairly good; abdominal and dorsal muscles were weak. Contraction could be obtained in most muscles on strong stimulation, but not in quadriceps or gluteal.

CASE 2.—Male, age 7, small at birth, legs always contracted; never able to walk. On examination limbs were thin and wasted; long hands and feet; face somewhat expressionless, eyes prominent, facial muscles act; unable to walk; arms thin and wasted; muscles small; all movements could be performed; legs thin; knees could not be straightened owing to contraction of ham strings. Most movements could be performed, but legs could not be extended; knee-jerks absent; all muscles reacted to a moderately strong faradic current.

CASE 3.—Female, aged 6; could not stand or sit up, but could remain in sitting position; could always move both legs and could pick up small things with either hand; was intelligent. On examination, small for age, eyes prominent, sat up if placed, or lay on back with knees flexed; feet and hands appeared long; knee- and hip-joints could not be fully extended; muscular wasting general; muscular sense normal, knee-jerk and plantar reflex absent.

SCHULLER.⁴ He demonstrated a child, male, age 19 months. The child was weak from birth. It learned to sit up and stand. After ten months, it was no longer able to stand nor to sit upright. On examination in addition to slight symptoms of rickets, there was a high degree of hypotonia of the muscles of the lower extremities, but without evidence of atrophy. There was absence of the deep reflexes; diminished electric excitability; active movements of legs could be carried out in but slight degree.

SPILLER.⁵ Male, aged 22 months. The condition was first noted at five months; has never been able to hold anything in hand; at entrance into hospital child was well developed for 20 months old; muscles not wasted, but soft and flabby. The limbs were moved voluntarily at all joints, but the movements were very weak. There was a remarkable range of passive movements of legs, the feet could be placed behind the head while the front of thigh was in close contact with the trunk. There were no patellar or tendon reflexes; irritation by pin caused motion. The child had been constipated since 2 months old, which was attributed to weakness of the abdominal walls. The muscles reacted to the faradic current. Autopsy: No rigor mortis; muscles flabby. On cutting into calf muscles a great deal of subcutaneous fat and little pale muscle tissue were found; in sole of foot muscle almost absent. Microscopically the muscle fibers were small and those from the foot smaller than those from the back. The transverse striation was normal, the longitudinal not so well marked. The brain, spinal cord, and nerves were normal; no degeneration by Marchi stain. Spiller regards an arrest of development of the muscles the essential pathologic condition. Smith gives a subsequent report on the examination of the thymus.

OPPENHEIM.⁶ Child (sex not stated), aged 1 year and 7 months; no hereditary trouble; soon after birth it was noticed that the child could not move its extremities though all the muscles supplied by the cranial nerves were normal. When 9 months old some movement of the arms was obtained, but the legs remained completely lame. The child was well developed and nourished. There was slight reduction in the volume of the muscles, which had a peculiar doughy feeling. There was diminution in the muscular tonus; the tendon reflexes in the legs were abolished, and the muscles did not respond to mechanical or electrical stimulation, with the exception of some feeble contractions in the peroneus.

BERTI.⁷ CASE 1.—Boy, 3 days old. Two days after birth it was noticed that with the exception of the eyes, lips, tongue, and head, there was no motion. He lay with stretched limbs, crying weakly. The breathing was shallow and frequent, of diaphragmatic character. All the muscles of the extremities and the trunk with the exception of the diaphragm seemed to have no function. There

was complete atony of the muscles. After three weeks the respiration was deeper. On stimulation there was slight motion of one arm. Subsequent history unknown.

CASE 2.—Girl, 5½ years old. On the day after birth it was noticed that the child, otherwise normal, seemed to show no life in the body with the exception of the head. After three weeks there was slight motion in one arm and in some of the fingers. After a year and a half the child could lift up the arms and there was slight movement in the legs. This condition lasted until 5½ years old, the child becoming emaciated. Now all movements are carried out slowly. She stands with legs spread out. The muscles are soft and relaxed. The electrical stimulation is diminished; knee-jerks sometimes doubtful; easily exhausted; no alteration in sensation, no sphincter trouble.

KUNDT.⁸ Child, 18 months old. No hereditary trouble; two other children are normal; the pregnancy and birth were normal. The fetal movements were felt just as in the other pregnancies; mother noticed no movements of feet from the first; after six months there were movements of feet and lower limbs; thighs remained motionless; child could sit up, but could not stand. The arms were normal. The child was well nourished; subcutaneous fat abundant; the muscles were extremely lax on palpation. All passive movements of the hip joints easily carried out, but some opposition to extension of lower leg. The knee-jerk was absent. The Achilles reflex appeared on the left, but was imperfect on the right. Electrical stimulation produced contraction of the lower legs. After three months' observation a slight improvement was noticed. There was never reaction of degeneration.

ROSENBERG.⁹ Male, 2½ years old. Family history negative. Mother did not feel fetal movements during pregnancy. Pregnancy and birth normal. Child nourished by bottle. The arms, head, face, and eyes moved normally. The child sat up at seven months. At eleven months on attempting to stand there was no strength in knees or hips. Child at time of report could not stand or walk. In other respects it was normal. The upper and lower legs could not be moved. The feet and toes could be actively moved. When a leg was lifted it fell as a dead weight. Contractions in the apparently paralyzed muscles were produced by pain. The legs showed no atrophy. There was entire absence of muscle tone and very extended passive motion could be made. The feet could be brought in contact with the ears. Palpation showed a decided difference between the affected and the normal muscles, the former having a soft doughy feeling. There was absence of knee and Achilles reflexes. There was complete absence of electrical reactions in the gluteal, in the quadriceps and in the adductors. In the lower leg only the peroneous gave a reaction. After six weeks' faradic treatment some improvement was noted.

IOVANE.¹⁰ Male, aged 3 months. Family history negative, normal pregnancy and delivery. Child appeared healthy and took the breast. On the first day it was noticed that there was no voluntary movement of the arms or legs and that the head rolled about on the trunk. When seen at three months, there was flaccid paralysis with absolute atony of muscles of arms and legs; feeble movement at wrist; muscles of trunk atonic, only abdominal reflexes present; slight response to faradic current, none to galvanic. Child died at five months with bronchopneumonia.

SORGENTA.¹¹ Both children by the same mother. No movements during pregnancy. In both clinical history about the same. Both well developed at birth and from birth unable to move arms or legs; absence of cutaneous and deep reflexes; no reaction in muscles of legs; weak in arms. Death in one on fortieth day, in other on fifteenth day. In both cases convulsions preceded death. No autopsy.

These cases of Sorgenta have been excluded by Collier and Wilson, chiefly in view of its familial type and classed with the myopathies.

COMBY.¹² Male, aged 8 years. When seen first in September, 1905, could neither walk nor stand; kyphosis on sitting; intelligence good. The only defect

was in the muscles, which were soft, but not atrophic; could move legs but they were not strong enough to support him.

CATTANEO.¹³ Female, aged 4 months. Birth normal. Fetal movements not felt. Breast fed. After birth it was noticed that the child could not move hands or arms. Father thought it could move arms at time of report. Could not hold head up. Observation showed a well nourished child; only slight movements of hands and feet; cutaneous and deep reflexes absent; electrical reactions diminished.

BING.¹⁴ Male, 3½ years old. A typical case. It was at once noted that the legs were passive appendages to the body and could be moved readily in all directions. A normal birth. Congenital bilateral pes varus. Great weakness of muscles since birth. Child could neither stand nor walk. Arms could be moved, but movements weak. Head could be held but a short time in one position. Knee-jerks absent, no disturbance of sensation or of sphincters. Bing removed a piece of muscle but does not state from which part and found it normal, although there might have been some question whether the nuclei were not more abundant than normal. He questions whether the condition is to be regarded as functional or due to a non-development of the spinal cerebellar tract which governs the tonus.

TOBLER.¹⁵ Male child, the first born. First observed at 20 months and under observation three years. Fed on breast for six months. From the first the loss of motion was striking. Examination at 20 months showed a well nourished child. All extremities in condition of complete atony but no paralysis; some motion in arms but slow and weak. Atony even extended to facial muscles, but the movements of tongue and eyes were normal; electrical stimulation greatly diminished and in part lost; sensation not affected; intelligence good; no change during continued observation for three years. Death probably from diphtheria at 5 years. No observation as to fetal movements.

VARIA AND DEVILLERS.¹⁶ First child; fifty-nine days before birth mother fell and was laid up with periostitis until eight days before birth. During pregnancy, both before and after the accident, fetal movements were felt; child under observation for nine months; female child; arms and legs immobile; all the muscles abnormally flaccid. The head rolled about indifferently when not supported. There was spinal kyphosis when child was seated, which disappeared on lying down. Death from bronchopneumonia when 9 months old. (Pieces of muscle and cord were sent to Dejerine for examination but no report has been published.)

COMBY.¹⁷ Male, aged 4 months. When one month old the child had an attack of diarrhea and it was then noticed that the muscles were paralyzed. When examined, legs immovable; no muscular wasting; knee-jerks absent; no support for head; electrical reaction showed hypo-excitability of right leg; no reaction of degeneration. After a year muscular atony persisted.

CARY COOMBS.¹⁸ Female, aged 10. Flabbiness of one hand noticed one-half hour after birth. Nothing further was noticed until time to walk. Then it was found that the legs would not support her; could not walk by herself until 2 years old; arms most affected; ankles often turned causing her to fall; extraordinary flaccidity of all joints; knuckles could be made to touch the back of the wrist; lower limbs very hypotonic, but not so much so as upper; knee-jerks and tendon reflexes were present; electrical excitability was diminished. Muscles could be distinctly felt, but they were small, soft and doughy.

LECLERC.¹⁹ Female, aged 4 years. Mother felt fetal movements as in the case of her other children. For the first days the child appeared normal. A bronchopneumonia developed at 6 weeks of age and after this the paralysis was observed. The child then appeared completely paralyzed, incapable of making any movements of extremities. Head falls on shoulders when moved. From this time a slow but progressive improvement took place. At the time of the report the child could move the limbs, but the movements were feeble. Not a true paralysis, but muscular atony. The face and all muscles innervated by cranial nerves were

normal. The passive movements of the joints were greatly exaggerated. The muscles were not atrophied, but seemed extremely soft. The intelligence was slow in developing.

BAUDOUIN.²⁰ Child, 4 months old, female. Pregnancy and birth normal. Since birth neck, trunk, arms, and legs were immobile. Muscles supplied by cranial nerves normal, except for slight internal strabismus of right eye; complete flaccid paralysis in trunk and limbs with the exception of feeble movements of fingers and toes; absence of deep reflexes; respiratory muscles were affected. The thorax dilated very slightly during respiration. Faradic excitability was diminished. Death from bronchopneumonia. (Baudouin says that the disease tends naturally toward recovery and if cases are met with early a complete recovery is possible, which is somewhat at variance with the results of his autopsy.) He found in the cord at the level of the eighth cervical segment that the cells of the anterior horns were diminished in volume but there was no evidence of neuron phagocytosis. He thinks there is probably an arrest of development. Section of the anterior and posterior nerve roots showed the anterior four or five times smaller than the posterior. The posterior stained more deeply than the anterior. In the anterior root the sheaths were more widely spaced and separated by amorphous tissue. Sections of the sciatic nerve stained with Marchi showed no fragmentation of the myelin. In sections stained by Weigert's the nerve was not well stained, the myelin sheaths were thickened and not equal in number in the different bundles. He concluded that with the myelinated fibers there were numbers of nerves not yet myelinated. The same lesions were found in the crural, cervical and median nerves. The condition in the nerves was not a neuritis but an arrest of development and a retardation of myelin formation.

The muscles presented very profound lesions, varying little according to the muscle examined. The connective tissue sheaths were numerous and thickened. The vessels were normal, but often surrounded by young cells. The muscular fibers were much changed. There were masses of small fibers from 6 to 8 microns in diameter and along with these very large fibers often reaching a hundred microns. The nuclei were increased in number and often lay in the interior of the fibers. The striations were normal and there was no degeneration. The diaphragm was the least affected. The skin was normal, the lungs showed disseminated bronchopneumonia. There was slight sclerosis of spleen with follicles more accentuated than normal. The thyroid gland was sclerosed and contained no colloid. There was sclerosis of the thymus with small Hassall's corpuscles. The condition was due to some cause which had suspended the development of the marrow and the nerves, and through these changes the muscle had become affected.

AUSSET.²¹ Female child, 2 years, 9 months old. Mother had five children, two born dead. No fetal movements during pregnancy. After birth the mother noticed that the child was unlike others. It was inert and lay five or six hours without demanding the breast; did not move limbs even when crying; there was slight movement of arms. At 18 months there was some febrile disturbance and at two years whooping-cough. On observation, nutrition appeared good; fat abundant on lower legs; slight movement of arms; legs immovable; no actual paralysis; when leg was lifted it did not drop as rapidly as would a paralyzed leg. The joints were not abnormally movable. The left leg was smaller than the right. The electrical reactions were normal.

BRUNARD.²² Child aged 2 years. External appearance was that of a well nourished infant rather deficient in fat. No hereditary trouble. Birth normal; fetal movements felt; breast nutrition. At the age of 2 months there were convulsions which had not reappeared. The first teeth were late in appearance. The attitude was striking. The child lay on her back, the legs flexed on the thighs, with total abduction. The extremities could be moved, but the child could not take hold of an object; could not walk; gave picture of child sitting down, the body bent forward, the face on the ground between the feet. The patellar reflex was absent; electrical reactions did not appear to be diminished; no trouble with

respiration, circulation or digestion. The child was idiotic. (In this last the case departs from the type, since all the other cases showed normal intelligence.)

COLLIER AND WILSON.²³ CASE 1.—Boy aged 4. Normal pregnancy and birth. No mention of fetal movements. At birth well-shaped but thin; breast fed. The position assumed naturally from birth was one of flexure of hip and knee and extreme dorsiflexion of ankle; legs and arms weak and limp; could not hold head erect. On examination, a small, thin, soft, limp child; muscles small and absolutely atonic, the joints so relaxed that the limbs could be placed into all sorts of fantastic positions without discomfort. The muscles have a soft, velvety feel. A limb held up by its proximal end can be shaken like a flail. There was contraction of the iliopsoas, adductors, and ham strings on both sides. With this restriction, all voluntary movements could be performed quickly and with normal range, but the power was very feeble. The vertebral column bowed in the sitting posture but the curve disappeared when the child was held by the shoulders. The soles of the feet were almost flat, soft and like long pads. Faradic and galvanic excitability was lowered. The deep reflexion without exception were absent.

CASE 2.—Boy, aged 7. The mother was weak in the limbs when a child, and several members of her family could not close the eyes properly. Birth normal. No mention of fetal movements. Soon after birth it was noticed that the child was unnaturally limp and could not hold up his head; had never been able to walk; slow improvement since three years old. On examination, head large, facial muscles weak, inability to close eyes properly; universal flaccidity and weakness; the muscles were soft and weak; impossible to differentiate muscle from adjoining tissue by palpation. All muscles contracted voluntarily, but too feebly to do any useful act. All reacted to faradic current. Child had a peculiar triangular face and open mouth which may have been due to maldevelopment or to muscular contraction preventing the full growth of the mandible. The superficial reflexes were normal, the deep entirely absent. There had been gradual improvement and when last examined the child could walk a little without support.

CASE 3.—Boy, aged 5½ years. Family history negative. Child breast fed. Nothing noticed for six months with the exception that the child placed his limbs in extraordinary positions. After this the mother noticed that the legs were weak. He finally was able to stand when holding on to something; then became weaker and weaker in the legs. On examination, a pale, thin child, of average height; intelligence good; no difficulty in speaking and swallowing. Muscles of upper extremities were small but all voluntary movements could be performed. There was absolute hypotonia of all the muscles, with relaxation of the ligaments and flail-like joints. Muscles of the neck and trunk were thin and weak. He could raise his head only when lying in the supine position and sat up with difficulty. In the lower extremities there was slight contraction of the flexors of the thighs and decided contracture of the muscles of the feet. The faradic excitability of the muscles was diminished. The superficial reflexes were normal; the deep, entirely absent. Continued improvement occurred.

CASE 4.—Girl, aged 1 year, 8 months. Family history negative; pregnancy and birth normal; fetal movements felt; breast fed; child normal until 12 months old. At this time she was ill for a month with an attack of bronchitis. At end of illness it was noticed that she could not move her legs; arms not affected. On examination, a thin but otherwise fairly developed child; motion of upper extremities normal, but weak and flaccid; the muscles of the lower extremities were absolutely atonic; movements very weak; considerable voluntary control; a flail-like condition of the joints; the deep reflexes were absent; the faradic excitability was diminished. After being at the hospital for three months marked improvement in the power of all muscles was noticeable. (The cases of Collier and Wilson are rather different from the other cases which have been reported, in the age of the patients, in the slighter degree of the muscular involvement, and the time after birth of the development of the condition.)

GASTONGUAY.²⁴ Child aged 3 years and 8 months. Mother perceived no fetal movements; nothing abnormal noticed for six weeks; then after a pulmonary attack the child appeared completely paralyzed with the exception of the face and pharynx. Child nursed and drank perfectly. When seen there was no complete paralysis, but atony of the muscles. This atony extended to the ligaments, rendering the joints much more flaccid and giving greatly exaggerated passive motion. The muscles did not seem atrophied but were much softer than normal. All muscles enervated by the cranial nerves were intact. The skin was not very supple, that of the lower extremities showed a hard, smooth edema. The mental development was retarded. Slight improvement occurred while under observation.

LEEBEBOULLET AND BAUDOUIN.²⁵ Child, aged 11 months. Flaccid paralysis having its maximum in the muscles of the neck. Head rolled unsupported. The extremities were equally affected; reflexes diminished but not abolished. Death, with fever and dyspnea, due to a beginning pulmonary septicemia. Convulsions were seen and during these the flaccidity gave place to contraction. Autopsy: The cord and brain were examined by methods of Nissl and Marchi. These were found normal. No diminution in size or number of the cells in the anterior horns. The muscle lesions were marked, particularly in the neck muscles. The fibers were of irregular size. The transverse striations were absent; the longitudinal present; a considerable increase in nuclei.

LAFFER.²⁶ Girl, aged 8 years. Birth normal. Soon after birth, it was noticed that the face was immobile; could hold head erect when a few months old, and sit up when 7 months; began to walk when 14 months old, but with a peculiar waddling gait. There had been slight improvement since. There was great flaccidity of joints, particularly those of the lower extremities, and muscular weakness. (This case offers differences from the other cases in the first appearance of the condition in the face. There was no note of flaccid atony in the lower extremities until she began to walk at the age of 14 months.)

ROTHMANN.²⁷ The first child of the mother. The mother fell on her back in the eighth month of pregnancy. Fetal movements were felt but were weak. When 14 days old the mother observed that it did not move the limbs, and thought the condition was present from birth. The child when seen at 4 months was a typical case. A badly nourished child of normal size. Skull, otherwise normal, showed closure of the large fontanel. The legs were relaxed and showed no trace of active motion. On the upper and lower legs the skin was thick, the fat abundant; the muscles could not be palpated. The legs could be moved in any direction without opposition. The skin and tendon reflexes of the legs were absent. The arms could not be actively moved. There was movement of the fingers. The head fell to one side or forward or back on the body when moved. The face, the pharynx, the tongue, the eyes, all moved normally. There was no paralysis of the sphincters. Electric stimulation procured effect only on flexors of arms. When crying the expression was normal.

Autopsy. The thymus was large for the age of 5 months. The cord was small and firm. Microscopically the cord showed extensive disappearance of the large motor ganglion cells of the anterior columns. The few motor cells which were retained were smaller than normal and showed evidences of degeneration. The absence of all fresh degeneration showed that the condition must have lasted several months. There was also a diminution of cells in Clark's columns. The white matter was entirely normal. In the vicinity of the hypoglossal nucleus there was chromatolysis and apparent beginning of the process. The investigation of the peripheral nerves of the arm and leg showed diminution in the size of the fibers, with thickening of the perineural connective tissue septa. There was no degeneration. The nerve fibers in the muscle were made out by the gold chlorid method; the end plates were not seen. Since according to the condition of the anterior horn cells only few motor fibers could be present, they must either have vanished without leaving a trace, or there must have been a regeneration in fetal life. The biceps showed increase of the connective tissue with increase

of nuclei. In the quadriceps there was infiltration of fat between the fibers with small-cell infiltration. The intercostal muscles were normal. The thymus showed an increase in the Hassall bodies and thickening of the walls of the vessels.

COLLIER AND HOLMES.²⁸ Child, aged 3½ years. Pregnancy and birth normal. No mention of fetal movements. Mother noticed that the child did not kick like other children, but no other peculiarity was noted until a year old, when she tried to stand him up and found that his legs doubled up under him; was never able to stand or to walk; could not himself assume a sitting position. The diaphragm and intercostals acted well. There was no local muscular wasting. Passive movements at all the joints was free, and flail-like movements of hands and fingers could be produced by shaking. In the lower extremities hypotonicity of muscles of thigh and calf. The feet could be easily touched together behind the head. Deep reflexes absent; superficial, normal. From this patient a piece of thigh muscle was taken for examination, as well as from one of the previous patients of Dr. Collier, who had died from bronchopneumonia. No mention is made of the examination of other tissues and there is no general account of the autopsy. The muscles were fixed in Zenker's and sections made. The muscles appeared very pale and infiltrated with fat. Very few spindles could be found in the more severely affected muscles. The majority of fibers were much reduced in size, and showed an average diameter not exceeding twelve microns on cross section; they were irregular in shape, the cross striation well preserved. The nuclei seemed to be largely in excess of the normal. A small number of fibers were enormously enlarged, up to 150 microns. Regressive changes were present in many of the hypertrophied fibers. There was great increase of connective tissue in the affected muscles. The muscle bundles were normal. The intermuscular nerve fibers were small. The muscle changes are the essential pathologic lesions. They may be regarded either as due to regressive changes in previously normal fibers, or as due to defective development. He gives photographs of the slides which show an almost identical condition with that seen by us, with the exception of the size of the fibers, that of the atrophic fibers being 12 microns. The autopsy description was limited to the muscles.

J. P. CROZER GRIFFITH.²⁹ At a meeting of the Philadelphia Pediatric Society Griffith showed a typical case in a boy about 17 months.

ASHBY.³⁰ Girl aged 8 years. Condition existing from birth. The patient lay in bed as if completely paralyzed. All muscles of the body, including face, were flabby and wasted; difficulty in masticating solid food; reflexes feeble; electrical reactions normal; all special senses normal. The condition gradually improved. (This case departs from the usual type in the involvement of the facial muscles and those of mastication.)³¹

SYMPTOMATOLOGY

The description of the disease first given by Oppenheim covers very well the main points in the symptomatology. All reports agree as to the flaccid paralysis, most marked in the lower extremities, and the general non-involvement of the muscles supplied by the cranial nerves. The only possible exceptions are a difficulty in deglutition in two cases, and in one an inability to close the eyes. The great flaccidity of the joints, which might be supposed from the condition of the muscles, is also generally described. No description of this can be better than that given by the mother of one of Collier's patients: "By whatever part of the body I held him up, all the rest of him hung down like so many pieces of yarn." When we consider the remaining symptomatology there is much uncertainty. Sensation in the affected parts seems on the whole to be unimpaired, but an abnormal tolerance of strong faradic currents has been

mentioned. The reflexes may or may not be present. Contractility is generally produced by the faradic current, and there is absence of the reaction of degeneration.

ETIOLOGY

There is no accurate knowledge of the onset of the disease, whether sudden or gradual. In all the descriptions it has been impossible to give any exact time so that the onset must have been gradual; possibly weakness preceding atony, and a gradual extension of the field; in some of the descriptions this is evident. Oppenheim and those following have laid weight on the congenital nature of the disease as being one of the important conditions belonging to it. Certainly this is involved in much doubt. It is true we know nothing of the time a muscle degeneration may be in progress before symptoms are produced, but if we assume that the beginning of the disease is coincident with the appearance of the flaccid paralysis, then it certainly is not usually congenital. Of all the cases, in but five it is stated that it was present at birth. An important point bearing on its congenital nature is that of the fetal movements of the child. The degree to which this is felt varies and its absence does not denote fetal paralysis. In the cases we have collected, the presence or absence of fetal movements is mentioned in ten. In these the fetal movements were felt in seven and were absent in three. The usual statements of the time after birth are vague. The time extends in one case to seven months, in another ten, in another twelve, and in one case seven years. In regard to the frequent cases in which the condition was noted from two to thirty days after birth, it does not seem probable that it could have been present from birth and escape the attention of the mother, the nurse and the physician. We have asked several obstetricians with regard to this and they have not thought it possible. The mothers who have been asked have with some heat denied the possibility, and have even regarded the question as an attempt to secure antisuffrage evidence by showing in the female gross deficiency in the powers of observation. In none of the cases has it appeared in connection with an acute infection. In four cases it is stated that it appeared after a bronchopneumonia, and after diarrhea in one. In view of the frequency of these conditions, there is evidently no relation. It is scarcely possible by symptomatology alone to make a disease entity. To that belongs first a proved etiologic factor, or in the absence of this, definite pathologic lesions.

PATHOLOGY

There have been six autopsies made on cases and in two additional cases examination of the muscles, and there is much disagreement as to the character of the lesions. In one of the autopsies by Baudouin there was diminution in number and degeneration of the anterior horn cells and absence of myelination in the nerves; in another, the case of Lere-

boulet and Baudouin, the cord and nerves were normal. In Rothmann's case there was marked involvement of the anterior horns and the nerves. In Spiller's case, in ours, and in one of Baudouin's, the cord was normal. Presumably it was also normal in Holmes' case, since he makes no mention of its examination.

There is much more unanimity in regard to the condition in the muscles. Spiller regarded this as due to imperfect development, and most descriptions mention the great diminution in size of certain fibers and the great enlargement of others. Holmes found fibers up to 150 microns in diameter, and Baudouin found fibers of 100 microns. The photograph which Holmes gives of a cross section of muscle certainly shows no such fibers and might have been made from a section of the muscle in our case. Bing found the muscle normal, though there might have been some question of a nuclear increase. Such variation in the anatomic lesions are akin to the variations in the symptomatology and are not sufficient to serve as a basis for the creation of a disease entity. Even in the case of the lesions in the muscles, there are a number of conditions which produce similar lesions, as the great atrophy of certain fibers with a normal condition, or an enlargement of others.

The condition of the thymus gland is interesting. It was found to be enlarged in Spiller's, Baudouin's, Rothmann's and our case. Whether there is any relation between the thymus and the condition is uncertain. We regret that no microscopic examination of the gland was made in our case. Spiller and Smith³¹ found fibrosis, enlargement of the Hassall bodies, endothelial proliferation, and arteriosclerosis. Baudouin found sclerosis with diminution in the Hassall bodies, and Rothman enlargement of the bodies with thickening of the walls of the blood-vessels. To any one who has made many examinations of the thymus, these statements do not convey anything. There is no organ in the body which varies so enormously in size as does the thymus in children under one year. We have taken from the records of the pathologic laboratory, Harvard Medical School, the weight of the thymus in sixty autopsies on children under 1 year of age and found a variation from 1 to 26.5 gm. The average is 4.5 gm. There is no record of weight equal to that of the thymus in this case, the next highest being 26.5 gm. in a child of four months with status lymphaticus.

There is no reason to believe that the disease is an infectious one. The onset, the distribution of the lesions, and the absence in our case of any changes which might show a past infection even, all speak against this. The lesions are not focal. Neither single muscles nor single muscle groups are affected. All the muscles innervated by the spinal nerves are affected though in different degree. The disease has further never been

seen in an epidemic or in an endemic form. The reported cases are generally distributed and have become more numerous in late years because attention has been more attracted to the disease.

It seems much more evident that the disease is toxic rather than infectious and that in certain cases, at least, the action of the toxic agent is either directly on the muscle fibers or on the terminal nerves or nerve endings. It also seems probable that such a toxin is produced not in the infant but in the mother. There does not seem to be any relation between the disease and any other disturbance in the child, no relation to food or digestive disturbances. Some of the children were fed on the breast, others on the bottle; generally the children were healthy at birth. It is perfectly possible to conceive of the presence of a toxin in the blood of the mother from the action of which she would be protected by the presence of antibodies. The toxic agent would be transmitted along with the protecting antibodies through the placental circulation. After the birth of the child the action of the toxin would not be counteracted by the antibodies which are no longer received from the mother. We can conceive of such a toxin acting either on the spinal cells or on the nerves or on the muscles, or on all three tissues, of its being constantly present in the mother's blood, which would be the case in the Werding-Hoffman³² familial type, or only temporarily present as in the cases of myatonia. It is, of course, difficult to explain under such an hypothesis why single muscle fasciculi and single fibers in a fasciculus should remain normal as in our case.

PROGNOSIS

The prognosis in these cases is doubtful. Without actual destruction of nerve cells there should be considerable capacity for regeneration, and improvement has been seen in many of the cases. We do not know, however, whether muscles so altered as these are capable of complete regeneration. The few reports of cases up to 10 years of age do not seem to give a very good prognosis. Of course much will depend on the extent of the lesions.

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