A FORM OF FAMILIAR IDIOCY WITH ATACTIC-CHOREO-ATHETOSIC MOVEMENTS

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(WITH THREE PLATES)

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I. CLINICAL PART.

By Professor W. M. VAN DER SCHEER.

I had the opportunity to examine four children in the same family, who all developed well until a certain age. Afterwards they were declining bodily and intellectually; finally they had to be cared for, being quite dement and bodily defective.

The symptoms and the course of the illness were very similar in all four. All fell ill at the age of 5 years. All became very soon dement, all had disorders of speech, incontinentia of urine and faeces. All the suffering began with characteristic disorders of ataxia. In all the disorders incoordination were intercurrent symptoms. Soon hyperkinetic movements and torsio-spastic movements were added to the incoordinated movements and every intention was followed by choreo-athetosic and ballistic eruptions in many muscles. The reaction on painful stimuli was the same.

In all four children atrophia of muscles was found, mostly at the lower part of the extremities. In three of the four (the younger one is not yet wholly developed at the moment) occurred a total paralysis of the lower limbs with a contracture in extreme flexion. In the not contractured muscles an intense hypotonia was found. Epileptic fits never occurred. Vision and audition were always intact. Fundus oculi was normal.

Three of the four children are still living and cared for in an asylum. One of them, the third of the four, died 18 years old of an acute pneumonia. The central nervous system of this man was given to Prof. C. WINKLER and the interesting changes found in it may become a basis to a discussion of the clinical symptoms of the disease.

Certainly the family-predisposition in this suffering was one of the principal features. Therefore we begin with the description of the family.

The paternal grandfather suffered, at the age of 30, from a paraplegia. We learned that he suffered from an affection of the spine and, 43 years old, he died in a surgical hospital. But we could not get the details of the affection he suffered from.

The paternal grandmother had been cared for in an asylum, but recovered. She died very old of a gastric disease.

The father of the children is a healthy man, a merchant. No abusus of alcohol. He had two brothers and one sister. The brothers are still living and healthy. The sister died of a heart-disease.

The mother of the children had a good health until she was 52. Then she died in four weeks of an acute diabetes. Of her two brothers one is healthy, the other died of t.b.c. There was no family relation between the

parents. Never before there was noted any illness, as the four children have got, though there has been a careful examination of the family.

From these parents were born:

1. MARTEN. Patient.
2. A young woman, who got poliomyelitis at the age of 5 years and she is now a healthy woman, though an atonic calf of the right leg has remained.
3. A young woman, died at 6 months.
4. KLAAS. Patient. 20 years, died of pneumonia.
5. A young woman, died within 6 months.
6. JOHANNES. Patient. 17 years.
7. GEBKE. A young woman. Patient.
8. A young woman, now 16 years, healthy.
9. A young woman, now 13 years, healthy.
10. A young woman, now 11 years, healthy.

We will now relate the historiae morbi of the four patients who are all dement at the time we write.

1. MARTEN, the eldest child, was born in time, got his teeth in a normal way, learned to walk and got clean and developed as a normal child until his 5th year. He went to school, but after a few days he was ill. He got in low spirits, wept at the slightest occasion. His movements became unsteady. Every intentional movement was accompanied by contractions in muscles not intended to move. The intensity of those movements became stronger as any emotion intervened. When bringing food to his mouth he made himself dirty. His speech was soon unintelligible, he was incontinent for urine and faeces and his intellect deteriorated in a very short time.

He had no interest in his surroundings and was dull. At the age of 10 walking and standing without aid was impossible and he came to the neurological division of the University-hospital at Groningen.

1919. The historia morbi teaches us that the speech of the patient was indistinct, monotonous, scanned and unintelligible. His muscle power was insufficient. The muscle tonus was low. The muscles of the foot, that could not make a dorsal flexion, had a nearly normal tonus. At the moment he sat upright, an ataxia was seen in the muscles fixing the skull to the trunk, together with a strong ataxia in all extremities. Seizing something, he could not manage his hands. Walking or standing without aid was impossible because the strong ataxia of the trunk, with a tendency to fall backward, prevented it. The gait was with legs wide apart, swinging, the swinging legs being lifted up very high. The tendinous reflexes were strong in all extremities. Cloni of the knee and feet were found.

The knee reflex could be delivered from an extensive part of the leg. On both sides BABINSKI's reflexes were found and the abdominal reflexes were very strong.

There were no disturbances in sensibility, no disorders in the function of the brain nerves, except the disorder of speech. Vision, audition, taste and smell were normal. No nystagmus. Pupil reflexes on light and convergency normal. Papillae nervi optici were perhaps somewhat white. The patient is dement, good-natured and cheerful, he understands badly the questions asked him. The BINET-tests cannot be used. The diagnosis which has been made was: Cerebellar heredo-ataxia in the type of PIERRE MARIE.

Gradually all symptoms of grave ataxia, disorders of speech and dementia deteriorated. After a few years the possibility of walking was lost, the feet were contractured on the calf, the limb in a flexion-contracture. Vision, audition, etc. remained good.

At the age of 24 years he again was with his three brothers and sister in the neurological division of the hospital.

Then the examination teaches us: There have never been fits. He is a disabled man, 1,5 M. long, the arms and the legs are very thin. The skin is very richly pigmented, most of all the head, neck and trunk. He is covered with hairs on the legs.

The penis is small, the scrotum and testis are normal. Lien and hepar are not enlarged. Organs in the chest and abdomen are normal. Blood pressure 120/80. No changes in the urine, no swollen lymphatic glands, no disorders in the blood.

The patient is always lying, with the lower extremities in flexion-contracture and plantar flexion of the feet. The brain nerves are unaltered. Vision and audition normal. Normal fundus oculi.

Grave disorders of speech; only a few words are spoken and he never speaks spontaneously. Speech is unintelligible, monotonous, scanned with a marked perseverance. If he answers a question, many extra movements in the musculature of the face are made.

Motility. Arms are mostly crossed over the chest, but it is possible to extend them. Severe atrophia in all muscles of arms and legs.

The legs are in extreme flexion, clubfeet (Fig. I*a*). Low tonus in the muscles, but the flexors of the leg are contractured. In the elbow, hand and fingers a hyperextension is in all joints possible. The legs are paralytic.

The muscle-power in the arm is very bad. If the patient is resting, no motion is seen, but if he intends a movement, involuntary contractions appear in the upper extremities, in the trunk and in the head. Besides the incoordinate movements of the arms, many other groups of muscles are acting. If the patient tries to shake hands, the mouth is innervated, both upper extremities are turned and are swinging in enormously and the fingers are seen in an athetoid movement. At the same time the trunk spins round the axis of the spine and the shoulder (of the outstretched hand) is turned upward (Fig. I *b* and *c*). The head is swinging and turning. The knees of the in flexiocontracture remaining legs are joined

together. All volitional movements of the patient are accompanied by the above-mentioned, non-intended movements. The expression of the face is rigid. Seldom a laugh occurs.

Sensibility is, as far as the dementia allows the examination, quite intact.

Reflexes. The reflexes of the radius and the biceps are present but slow. No reflexes of triceps, of the knee or of the Achilles tendon are found. No cloni. No reflexes of the foot-sole. Percussion of the left tendon of the knee may produce a contraction in the right adductors and vice-versa. Percussion of the skull may produce momentary and sudden contractions of the face and the shoulder, as if the muscles were irritated.

Autonomic functions. A slight salivary stream. Incontinentia urinae et alvi.

Lumbar puncture. No disorder. Only the Gold-sol test is 0246532000.

Basic metabolism. 12,6 %.

Sugar in the blood. Normal.

Examination of the function of the liver. No alterations in GOUDSMIT's tests. The galactose (BAUER) test normal. EILBOT's test on bilirubine normal.

The patient is very dement. Most of the questions asked him he does not understand. He knows the surroundings and his family. He recognizes simple objects, which he uses and nominates them. Sometimes he has fits of screaming during a long time.

2. KLAAS. Age 20 years, born in time, was a normal child until he went to school. He remained there only a few days, because he was ill. He never has learned reading, writing or arithmetic. At the age of six, different uncontrolled movements were made at each occasion that he tried to make an intended action, and still stronger if any emotion occurred. Examined in the neurological clinic, a nearly photographically equal illness was found as in his brother MARTEN. There were not yet mental disorders. He was however initable, wept at the slightest occasion and did not govern his movements. It became soon difficult for him to take his food or any object near him; he had a swinging gait, lifting his feet wide above the ground and he often dropped down. By examinations all signs of locomotor and static ataxia in extremities and trunk were found. The speech was unintelligible, monotonous, broken and scanned.

The tendinous reflexes at the extremities are very strong; cloni at the knee and foot are found. BABINSKI's reflex on both sides.

There are no disorders in sensibility or in the brain nerves. The pupils have normal reactions; no nystagmus; fundus oculi normal; no fits. No changes in vision, audition, smel or taste. Incontinentia urinae et alvi.

Soon the disorder of speech grew worse and speech nearly disappeared.

The intellect was lost more and more and he became totally dement. Constantly he was incontinent. He could no longer walk and soon the patient, sitting in bed or in chair, had to be helped in everything. Some-

times, when lying in bed, he rolled round his longitudinal axis. The course of his sufferings was indentical with that of MARTEN.

In 1933 KLAAS was observed again in the neurological clinic of Groningen. Then was found: A young man, dement, destitute, very exhausted, with atrophied extremities.

Skin with much pigmentation at the head, neck, shoulders and legs. Beneath the hips a strong growth of hair. A small penis, normal testis and scrotum. No enlargement of spleen and liver. Organs in chest and abdomen normal. Slight albuminuria. No disorders of the blood. No swollen lymphatic glands. Large tonsillae.

The patient lies in bed with contractured legs, strong lumbar lordosis, the basin is lifted vertically and the chest is turned downward. Usually there is seen a tonic laugh in the face (WILSON's laugh. Fig. II *a* and *b*).

Nerves of the brain. No difference from the normal. No nystagmus. Fundus oculi normal. The lower jaw is always in action, making movements of mastication. The tongue is always moving, performing large movements in all directions. In the musculature of the VIIth Nerve are seen many occasional contractions, after an intentional effort. There is no longer any speech, sometimes a sound is uttered.

Motility. All muscles, especially those of the extremities, are strongly atrophied. The lower extremities are intensively contractured. Extreme flexion of the hip. The calf touches the back of the thigh. The feet and toes are in a maximal plantar flexion. The arms are hold partly flexed, partly in a gyrated position. If the patient is laid on his back, he immediately turns himself in a way that the chest touches the bed (Fig IIa). The muscles are weak, no tonus, and it is difficult to differentiate them from the surrounding tissues. As soon as the patient makes any volitional movement, it is not only incoordinate, but there occur both gyrating movements of the trunk and also swinging movements in the extremities with intense issue, and again the tongue moves, hand an fingers produce choreo-athetosis. Without any obvious volitional effort the patient is often seen in a gyrating movement. All joints of the upper limbs may be hyperextended by passive efforts, especially the hyperextension of the fingers may be extreme.

With the lower extremities no active movements can be made, but everywhere in the body the muscle power is small. If the patient sits up (only possible with assistance) the abdomen becomes prominent. The head may still be lifted from the pillow but powerless. Any coordinate movement is impossible. All active movements are complicated with swinging movements of the upper extremities, gyrating movements of the trunk, choreo-athetosis in the fingers and contractions in the muscles of the face, which however always retains its tonic laugh.

Sensibility. The patient is too dement to examine sensibility. Pain stimuli, however, are always accompanied by many large unconscious movements as described before.

Reflexes of the radius, biceps and triceps are found not exaggerated. No reflex of the knee. Reflex of the tendon Achilli is low but present. Also the abdominal reflexes. No cremaster-reflex. No reflex of the planta pedis.

Autonomic functions. Incontinentia urinae et alvi. Liquor cerebro-spinalis normal.

The test of the Goldsol 0134310000.

Basic metabolism ± 3 %.

Electric Examination. In all muscles, even in the most atrophied ones, normal reactions were found. The MM. biceps, pectorales and peronaei were examined. No degeneration-reaction was found.

Test of the liver of GOUDSMIT, BAUER and EILBOT normal.

Psychic Status. Totally dement. Only reactions of delight or pain are seen. No attention, understands nothing. No contact can be found with him. He opposes all efforts to correct his gyrated attitude.

3. JOHANNES. 17 years old, was the 6th child of the family. Born in time, his history is nearly identical to the history of MARTEN and KLAAS. At the age of 4 years the first symptoms of the illness were seen. The father remarks that his knowledge of the disease of the two other children made him see sooner that JOHANNES was also suffering from it. The first symptoms were an uncertain gait, soon followed by incoordination in the movements of the arms. Extra-movements were seen, augmenting after intentional efforts or emotions. The patient walked on his toes, but walking soon deteriorated and became impossible. His legs became flexed in the hips and in the knee-joints; the feet took an abnormal position toward the calf. The intellect deteriorated, speech became difficult; soon only unintelligible sounds were uttered. Incontinentia urinae et alvi.

The examination in the neurological division of the hospital shows us: A defective boy, with euphoria, good-humoured expression of the face, thin arms and legs, because they are atrophied. Pigmentation of the skin, of the head, neck, coccyx and organa genitalia. The legs are very hairy, the genitalia well developed.

No swelling of lymph glands. Tonsillae magnae. Organa of chest and abdomen are normal. Blood normal WASSERMANN. Bloodpressure impossible to determine, because the extensive movements. The patient lies in his bed with contractured legs, but he is never quiet, always in motion. In sleep, however, no movements are seen.

The nerves of the brain are without disorders. Fundus oculi with a slight peripheric pigmentation. Papilla optica normal. No nystagmus. Normal reactions of the pupils. In laughing there appears a persistence of the movement, a laugh of WILSON (Fig. III*d*). Percussion of the skull is followed by a rapid and intensive contraction of all muscles of the face and the neck, as if caused by terror; often also the shoulders and the whole body are contracted and the musculature of the face remains in the tonic

laughing contraction (Fig. III *b*). Though the boy hardly ever answers a question, his speech is monotonous and scanned. A few words, often repeated several times, like "water", "lekker", "broeder", are heard. Often the boy makes hissing sounds.

Motility. The muscles of the extremities are very much atrophied. The legs are always in flexion, the foot are clubfoot. It is impossible to move the feet, but is is possible, to a certain extent, to move the thighs and knees. The forearm is gyrated at the upper part of the lower arm and has a valgus-position. The calves are very atrophic. All muscles are hypotonic and cannot be differentiated from the surrounding tissues. All joints of the upper limbs may be hyperextended. Hyperextension of the fingers succeeds in a maximal degree. The muscle power has lessened in the extremities, mostly in the legs. It is impossible for the boy to sit without support; standing and walking is also impossible. Every intentional movement or any other reaction, f.i. on pain stimuli, is followed by an atactic moving of the muscles, but also by incoordinate contorsions and oscillating movements with hyperextended position of both upper extremities. Large stretching movements as are seen in ballisme, appear and the trunk gets a turning movement (Fig. III *c*). If the movements are strong, even the lower extremities make turning and beating movements, so far as they are permitted by the existence of contractures, but, if so, the upper ones are making beating movements of an enormous issue.

These involuntary movements are spreading even in the musculature of the face and neck. The mouth is then often enlarged into a grin, but also other movements may appear around the mouth (Fig. III *a*, *b* and *c*). At the same time the fingers make athetoid movements, but not very strong (Fig. III *d*). It is hardly possible to form a judgment on the existence of the ataxia, because it is masked by the extra-contractions.

Sensibility. It is not possible to examine the boy on his sensibility. Only painstimuli produce the same enormous motor reactions as we described after volitional and emotional impulses.

Reflexes. All tendon reflexes of the legs are absent. In the arms they are high. No abdominal reflexes. Small flexion of the toes after stimulating the foot sole. If the head is brought upward, the back grows stiff as a poker.

Autonomic functions. Incontinentia urinae et alvi.

The lumbar liquor has WA.——, goldsol test 1345400000.

Tests of the function of the liver. GOUDSMIT, BAUER and the bilirubin-test of EILBOT are normal.

Intellectual Status. The boy is dement, not so dement as his brother KLAAS. He is euphoric, makes a playful impression. It seems as if he actively contemplates his surroundings. Questions or orders are not answered. He cannot fix his attention on any thing. If his orientation is defect, or if other disorders exist in his processes of thinking, they cannot

be stated. All his reactions are unintelligible sounds or a tonic laugh, if one is playing with him.

4. GEBKE. A girl, the only female with the same illness as her three brothers, was fully normal after birth; at 5 years of age different singular movements appeared. She went to school, but could not follow the lessons. Her decreasing intellectual capacities prevented it. It cannot be told by the family, which of the two functions changed most for the worse: either the dementia or the incoordinate actions. The parents only know that the illness proceeded in the same manner as in the brothers. She never had fits. Gradually she became atonic, without sufficient muscle power in arm and legs and stumbled at everything.

The somatic and neurological examination in the hospital shows: A fat girl, with a strong panniculus adiposis everywhere, but not at the forearm and the lower part of the leg, lies in bed without contracture of the lower extremities.

Normal hairgrowth. Mammae well developed, with small mammillae. Large tonsillae. No disorders in the chest or in the abdomen. No abnormal pigmentation.

Brain nerves. No disorders. No nystagmus. Pupil functions normal. Fundus oculi normal. Vision and audition intact. There is a dysarthric speech, not controlled, scanned. The expression of the face is euphoric. She often laughs and there is a maximal tonic reflex in the mimical musculature, somewhat resembling the laugh of WILSON.

Motility. The lower parts of the arms and of the legs are very thin. Compared with the upper parts, which are very thick, they have a poor aspect. Low tonus in the muscles, little plasticity, hypotonus. The patient is always in motion. At the upper extremities athetosic movements are seen, with hyperextension in the hand and fingers. Sometimes very strong involuntary and rude torsion-movements are seen (often when she laughs). Sometimes the patient in walking falls, as she crosses the lower limbs much too far over each other. In active movements it seems as if other impulses interrupt the undertaken movement; f.i. the lifting of the arms is suddenly transformed in a movement of crossing the arms (IV *b*). In all movements dysmetria is seen, with a certain incoordination, but at once another movement intervenes, other muscles are innervated and often the head is thrown backward (Fig. IV *c*). She cannot stand. She walks with an atactic gait, with intercurrent contractions. She may go down, but at the same time another movement tries to lift her up. She has genua valga et recurvata. In laughing she has a laugh of WILSON (Fig. IV *a*).

Sensibility is undisturbed.

Reflexes. The tendon reflexes of the upper extremities, as well as of the knee are brisk. Plantar reflex of STRÜMPELL. To the percussion of the skull is responded by strong and sudden contractions in the musculature of the face, neck and shoulders. The mouth is drawn backward. To

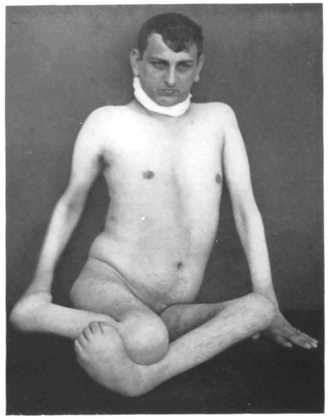


Fig. I*a*.

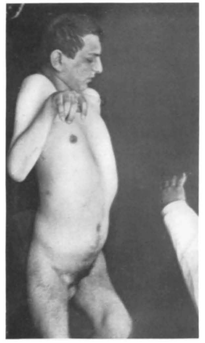


Fig. I*b*.

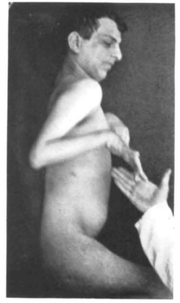


Fig. I*c*.

Fig. II*a*.

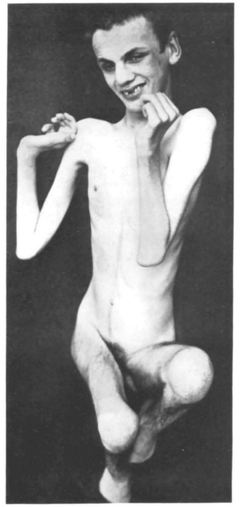


Fig. II*b*.

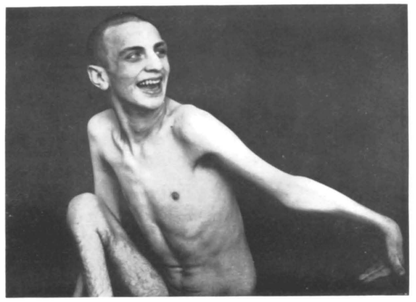
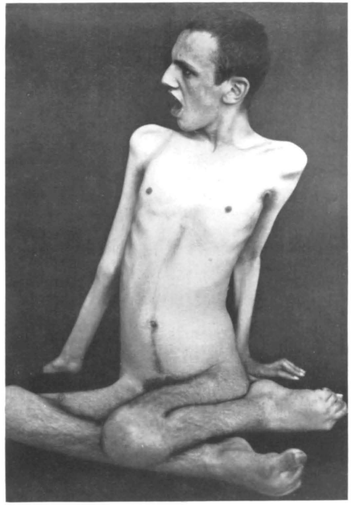
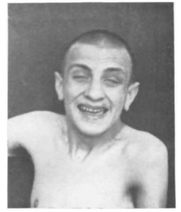


Fig. III*d*.

III*c*.



III*a*.



III*b*.

Fig. IV*a*.

Fig. IV*b*.

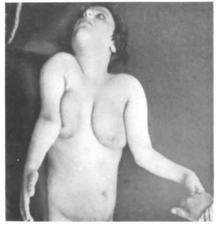


Fig. IV*c*.

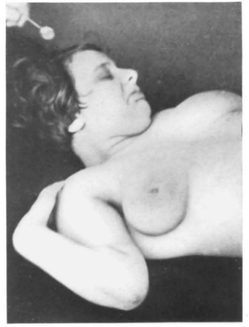


Fig. IV*d*.

the mechanical stimulation of the muscles she responded energetically.

Autonomic functions. Incontinentia urinae. Cerebro-lumbar liquor normal. Gold-sol test is 00232100000. The curve of glycose in the blood after 50 Gr. of glycose is too high and retarded. It is normal after 5 Gr. of glycose. The curve of galactose is normal. EILBOT's test of bilirubin too slow.

Intellectual Status. The girl with many psychic symptoms is not so dement as her brothers. She talks the whole day and a part of the night as a baby with palilalia. Her store of words is poor, reiterates mostly what is told her. Content and quiet, she does not understand her situation. She answers without understanding; if the question is complicated, she reiterates. Numbers are not conceived. She gives false informations about her surroundings and about her own person. She cannot find her bearings as to place and time. Her memory is bad; after a few moments she does not know what she has had for dinner. All impressions are soon forgotten. Short questions are sometimes answered by a short word. All associations are infantile on a low level. There is hardly any function of thinking. She rambles from one object to the other. She does not conceive abstract ideas. When playing, she is annoyed by many involuntary movements and makes grimaces. Her temperament is euphoric and she makes the impression of a baby, a very young baby, talking always, day and night, without aim.

Now, balancing against each other all the symptoms mentioned in the preceding historiae morbi, we may ascertain that there is not only an agreement in the symptoms of the illness, but there exists a nearly identical course in all patients. It may be that a difference in the intensity of the disorder could be found, but the essentials of the disease were alike in all patients. The similarity was so great that it seems possible to interchange the historiae morbi of KLAAS and of JOHANNES.

Psychical disturbances. One of the remarkable features of all sufferers was "a progressive dementia", beginning at the age of 5 years, whereas the psychical development in the first 4 years was absolutely normal. The first symptom of this dementia was a change in temperament. The high-tempered children became mourning, troublesome, variable in their affects. Afterwards we observe a slowly progressive, every year greater loss of all psychical functions. In the youngest, GEBKE, we observe a beginning, not yet total dementia. All they have learned is lost. The attentiveness, the possibility of impression upon memory, the formation of judgement, the impression of affects —, all is lost. All initiative, all spontaneity decrease and at the end disappear. At last a dementia remains, without any contact with the patients.

Disorders of speech. Together with the decline of the psychical functions speech deteriorates. First slowly progressive dysarthric disorders are found. Soon we observe a monotonous, pushing and stumbling speech. Afterwards it is no longer possible to understand the patients. Their store of words diminishes and at the end sounds only are uttered. The intensity of the

disorders differs in the patients. The eldest is still able te speak a few words. He nominates simple objects. KLAAS utters unintelligible sounds. JOHANNES did not speak as reaction, but sometimes repeated a few words persevering, in an unintelligible way. GEBKE had the smallest disorders in speech. Her speech was disarthric, monotonous and scanned. Her torrents of words with palilalia, her chatting and babbling without purpose and repeating over and again, were striking, as well as her iteration and imitation of speech.

Motility. Most interesting are the disorders in motility, opening the disease in all 4 children at the age of 5 years. They had learned walking normally. At that moment the gait became uncertain, they were soon exhausted, they lifted the feet too high and stamped, walked with legs wide apart, and after a year they could no longer stand or walk without help. In the arms existed atactic movements, when seizing any object. In eating they became dirty and, if they tried to catch anything, their hands went beside the objects. In the beginning there was a static as well as a locomotor ataxia; in standing and walking an ataxia of the trunk was seen. Soon involuntary reactions accompanied the intentional movements, growing in intensity by emotion.

At the age of 10 and 7, the two elder members of the family were, 16 years age, examined in the clinic and classified as cerebellar heredo-ataxia.

Afterwards a pes equinus appeared. The children walked on the toes. Every year the ataxia became more intense and the muscle power diminished. Gradually they could no longer stand on their legs; at first they were paretic afterwards paralytic. Together with the loss of muscle power there appeared contractures in plantar flexion of the feet and the toes. In two of the boys appeared a pes varus, in one a pes valgus. The fotos demonstrate them clearly. But at the same time extra-movements occurred in the arms, in the trunk, in the neck and in the face. *In their sleep they were quiet.* The extra movements, existing in a lower degree in the eldest brother MARTEN, appeared as a rough, gyrating, inappropriate choreo-athetosic movement, in the muscles which he intended to move as well as in other muscles. The direction of the movement is often interrupted, sometimes by a movement in quite another direction. Sometimes the extra movements are so intense that the examiner must be careful not to be injured by such a sudden movement in an opposite direction. It may be that the patient, trying to shake hands, suddenly crosses both arms over the chest or that one arm is brought around the neck and he stands in extreme abduction with the hands hyperextended and the fingers extended along the trunk. At the same time the trunk makes strange, revolving movements around the longitudinal axis of the body to the right or to the left side, the flexed legs are adducted, the head is turned in every direction, even backward, and in the muscles of the face appear many extra movements. The expressive movements may be very queer. The lips may be pursed, the mouth wide open or in another position, sometimes grinning, sometimes in a

jovial, but always rigid laugh. In KLAAS also the mandibular musculature and the tongue assisted in the extra movements.

The described ballistic, gyrating and turning unintentional movements were soon prevailing over the atactic movements and masking them. They all, however, had a choreo-athetosic character. The turning movements of the trunk were most explicit in KLAAS but were also found in MARTEN, JOHANNES and GEBKE. All hyperkinetic movements disappeared in sleep. They were seen after every order to move or on intention to move. Even GEBKE and JOHANNES showed them without any intention, as if those movements were spontaneous. JOHANNES and GEBKE were always so much in motion that examination became inpossible. Also after stimuli. Pain stimuli always brought about the trunk gyrations and the making of grimaces. GEBKE made them even as she laughed. Afterwards the muscle power lessened, not only in the legs, which were paralysed and contractured, in the three elder brothers. The muscles in the arms, the trunk and the abdomen became paretic and the patients could no longer sit in their beds without support.

The muscles of the neck also became paretic. In the youngest, GEBKE, there are not yet contractures of the legs, but there is the beginning of an equino-varus position of the feet.

Tonus, plasticity. Together with above-mentioned disorders in movement, position and bearing of the trunk and the extremities we find a marked muscle-atrophia in the three eldest patients. The muscles are hypotonic and palpation cannot distinguish their form. The plasticity of the muscle is nearly nihil.

Shapelessness, hypotonia and decreased plasticity also are found in GEBKE, mostly in the forearm and in the calf of the leg. The atrophia is not so marked, because of the adipositas. In her brothers the musculature of the extremities is strongly atrophied. In KLAAS and in JOHANNES the atrophia is very intensive. All the joints of the arms, hands and fingers may be hyperextended. In KLAAS, though the atrophia was marked, no reaction of degeneration could be found. In GEBKE the mechanical irritability was intense.

Resuming once more all disorders in the motility we have seen: Gradually all muscle power is lost in a few years, most in the lower extremities, suffering from a complete paralysis, hypotonia, low plasticity and atrophia of the muscles, without reaction of degeneration. Moreover, there was in the beginning a locomotor and static ataxia, in following years masked by swinging, ballistic and choreo-athetosic movements in the trunk and in the extremities, whereas the expression of the face was characterized by grimaces and the laugh of WILSON.

Autonomic functions. Very soon in the historiae morbi incontinentia urinae et incontinentia alvi is registered. In GEBKE only incontinentia urinae.

Tendinous reflexes. There are many signs of agreement in the behaviour of the tendinous reflexes of the patients, but also many differences. Some-

times they were absent in the legs, sometimes they could be found. But the presence of contractures often made it impossible to value the abscence of the reflexes. In the two eldest patients they were very high. Even cloni were present. In GEBKE the same was found. BABINSKI's reflex is registered in the beginning of the illness in MARTEN and KLAAS; afterwards this reflex was absent. The abdominal reflexes were found in all four; they were strong in the case of GEBKE, low in the other patients. Stress must be laid upon a glabella-reflex, found in all four, most exquisite in GEBKE and JOHANNES. Percussion of the glabella was followed by a sudden contraction of the muscles in the face, neck and shoulders; the mouth took a laughing or a whimpering aspect (Fig. III *b*, Fig. IV *d*). The whole was very sudden, as if the musculature was frightened, or as if the muscles were suddenly touched with an electric stimulus and brought in an agitated movement.

Sensibility was not altered. In GEBKE, not yet so dement that she did not answer questions, no loss or disorder in sensibility. Her reactions on centripetal stimuli were strong, not only on pain stimuli, but also on visual and auditory stimuli.

In the other three the dementia did not permit examination. Only pain stimuli were followed by strong excessive preventing movements, described above.

The cutis was strongly pigmented at the head, neck, shoulders, hip and genitalia.

The legs were very hairy, the tonsillae very large.

Negative Symptoms. There were no fits of any kind. Vision and audition remained unaffected as far as it was possible to verify those functions because of the dementia. There was no nystagmus and all pupil reactions were present. The fundus oculi did not present any alterations. A little pigmentation in the periphery of the retina was found in MARTEN and KLAAS. No ring of KEYSER—FLEISCHNER was found along the cornea. Liver and spleen were not enlarged and with the usual tests no deviations were found. WASSERMANN's test was negative.

II. PATHOLOGIC-ANATOMICAL PART.

By Professor Dr. C. WINKLER.

Professor Dr. VAN DER SCHEER kindly sent me the central nervous system of KLAAS, the second of the sufferers from heredo-ataxia, who, 20 years old, died of pneumonia. The symptoms of his disease are amply discussed by Prof. VAN DER SCHEER in his clinical study.

Even a superficial observation of the brain of KLAAS makes it obvious that the most striking feature is the enormous atrophia of the cerebellum. In normal cases the cerebellum surpasses by nearly one c.M. the occipital borders of the brain-hemispheres. In the case of KLAAS the occipital borders of the hemispheres surpass far the borders of the cerebellum. They are for circa 5 c.M. covered by the boundaries of the hemispheres. In this way it may be told that the cerebellum has lost perhaps $^9/_{10}$ of its volume (fig. 1).

I now will describe the microscopic findings in this cerebellum, the medulla and the other parts of the nervous system.

MICROSCOPICAL EXAMINATION.

A. The cerebellum.

Sections made through different parts of the cerebellum and stained with different methods make it obvious that the cortex cerebelli has very much changed.

1. The lamina molecularis is very small, reduced to the third of this layer in the normal cerebellum.

2. All cells of PURKINJE have disappeared (Fig. 2*a* and *b*). They are nowhere to be found, neither in the flocculus, nor in the hemispheres or vermis. They are always missing. Exceptionally there may be found a cell of PURKINJE, but only as a degenerated, swollen cell (to 3 or 4 times the normal size of the cell, Fig. 3). There are, however, not found any lipoid enclosures in the few swollen cells which were seen.

In preparations stained by BIELCHOWSKI's method it appears, however, that the longitudinal fibre-layer in the deeper part of the lamina molecularis is very rich in fibres (tangential fibres) and unchanged. Around the holes, in which PURKINJE's cells now disappeared, once have lain, very nice fibre-baskets are seen (Fig. 2 *b*), without any defects.

3. The lamina granularis has not changed at all. The granula-cells have not decreased in number.

The loss of PURKINJE's cells is followed by the loss of distinct fibres.

1. *lost* are the fibres going from those cells towards STILLING's nuclei.

There they are ending. In the three lateral nuclei, the nucleus dentatus, emboliformis and globosus are normal cells. Afterwards we return to the nucleus fastigii.

2. *lost* are also the systems that are called "the reticule-olivary cerebellar systems" (Fig. 4*a* and *b*). In their most distal part, in the nuclei lateralis tegmenti and in the nuclei olivares inferiores all cells have disappeared. The fibres originating from those cells are lost. They cross the inter-olivary part of the pars medialis substantiae reticularis, subsequently they traverse the descending tract of the N.V. in two or three pedunculi (MINGAZINI). Of all those fibres none are present and the field in the corpora restiformia, where the reticule-olivary fibres are found, is a field quite empty of fibres (Fig. 4 and Fig. 5).

There may be ascertained a very sharp contrast between the total degeneration of all cells in the olivary nuclei and the absolute intactness of all cells in the nuclei pontis.

The loss of PURKINJE's cells and with them the loss of the climbing fibres, surrounding them with their terminations is the cause of the degeneration of cells in the distal part of the reticular- and in the olivary nuclei, for the climbing fibres take their origin in those nuclei (Fig. 5). If it were still necessary to prove this well-known fact, here will be found the demonstration by a natural experiment that the climbing fibres take their origin in the cells of the two here named nuclei. They disappear together with the climbing fibres.

On the other side the nuclei pontis are found absolutely healthy, for the lamina granularis is sound. The nuclei pontis give origin to the moss-fibres, taking their course through the bracchia pontis and ending in the noduli of the lamina granularis.

Now returning to the nuclei fastigii, we have found all cells which they contain swollen and degenerated. But there exist sound arcuate bundles of RISSIEN RUSSEL.

Resuming: In the cerebellum all the cells sending centrifugal fibres to the medulla, f.i. the cells of PURKINJE, are lost, together with the whole reticulo-olivary systems. The cells of the nuclei fastigii are strongly degenerated without the degeneration of the bundle originating of those cells. *Only cells sending fibres in a centrifugal direction have changed.*

B. The medulla spinalis.

With the naked eye a contrast is seen between the atrophied ventral roots, which are small, and the strong, well preserved, dorsal roots. Only one exception is seen. The XVth posterior root is degenerated and its degeneration may be followed in the dorsal funiculus from the entrance of this root till the nucleus of BURDACH. With this exception all the funiculi of the spinal cord are normal. The ganglia intervertebralia did not came in my possession.

The motor cells in the ventral horns as well as in the nuclei intermedio-

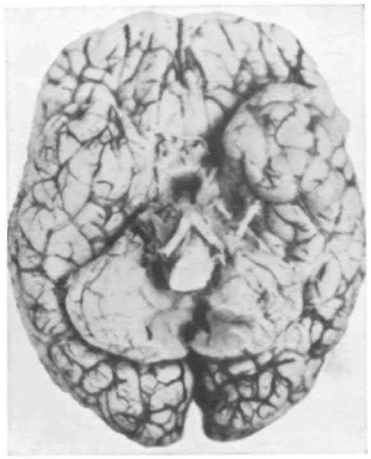


Fig. 1. A foto of the atrophied cerebellum.

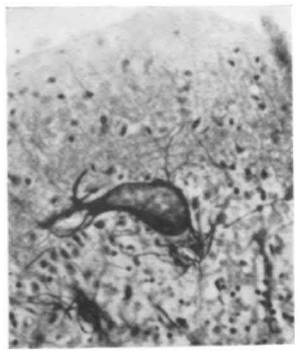


Fig. 3. A swollen cell of PURKINJE in our case. (BIELCHOWSKY's method.)

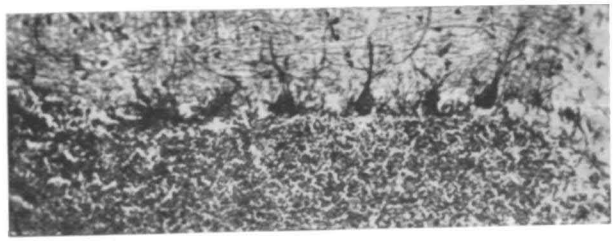


Fig. 2*a*. A foto of normal PURKINJE-cells. (BIELCHOWSKY's method.)

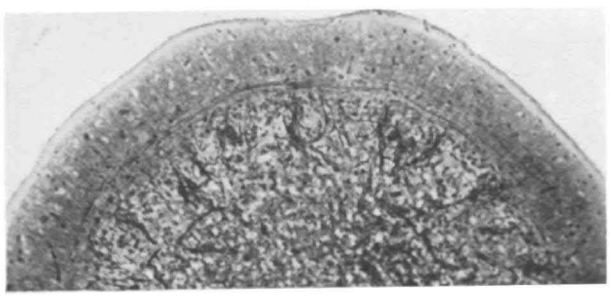


Fig. 2*b*. A foto of the loss of PURKINJE-cells in our case. (BIELCHOWSKY's method.)

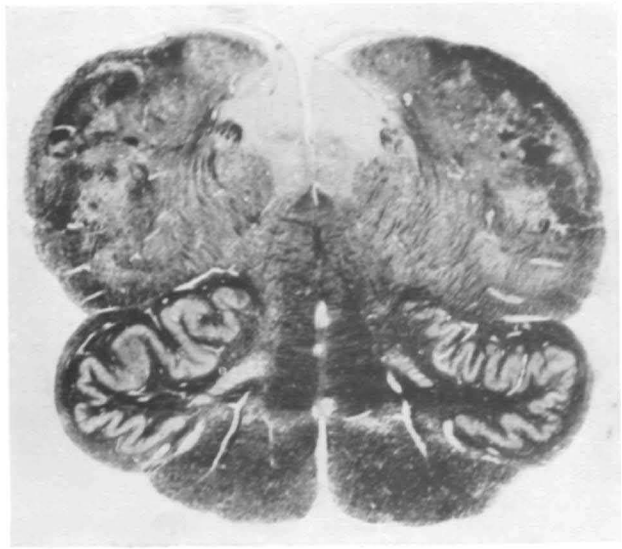


Fig. 4. A section through a normal medulla oblongata. (WEIGERT-PAL method.)

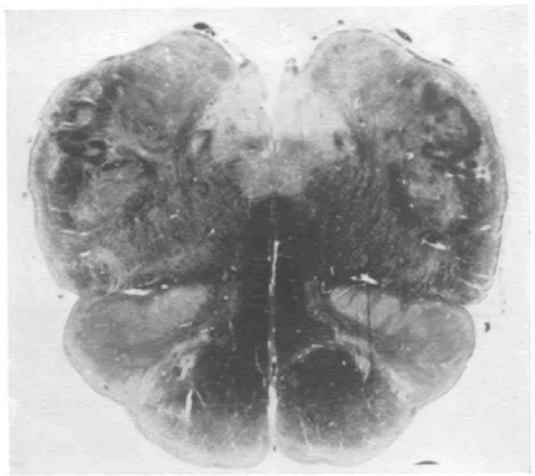


Fig. 5. Section through the medulla, where the tractus olivo-reticulo-cerebellar path is lost. (WEIGERT-PAL method.)

laterales have all disappeared in the *lumbar enlargement* and in the *sacral* and the *thoracic part* of the medulla. In the cervical intumescentia mast cells are lost, but a few swollen cells remain. The remaining cells are swollen, the cell nucleus is found along the margin of the cell, surrounded by a part of the tigroid (Fig. 6*a* and *b*). The swollen cell is filled up with a clear substance, taking no stains except a slight blue stain of cresyl-violet. They do not contain lipoids, neither with SOEDAN or with Nile blue. Often it is seen that there does not exist a distinct contrast between the swollen cells and their surroundings. It seems as if the cell is losing its boundaries, is bursting, and disappears in this way.

Resuming all we saw in the medulla, we may draw the conclusion: All larger cells in the medulla have disappeared or they are degenerated, swollen. Only in the cervical part sometimes a more or less normal cell is found. In the sacral, lumbar and thoracic part all cells have disappeared and the very few remaining cells are swollen cells.

C. *The motor nuclei of the brain nerves.*

In all the nuclei of the motor brain nerves the cells have more or less changed, though less than in the medulla. In the nucleus N. XII many cells are swollen but there are normal cells found also. Those nuclei are better as the spinal horns. In the swollen cells the nucleus is found at the margin with a rest of the tigroid substance (Fig. 7); a few normal cells are found in the motor nuclei of the NN. IX, X, and XI. In the nucleus of the N. VII (Fig. 8) cells are swollen, but there are more normal cells than in the nucleus of the N. XII. In this nucleus the change is intense. All the swollen cells are comparable with those, which are found in amaurotic idiocy. The same is the case in the nucleus of the VIth Nerve (Fig. 9) and in the motor nucleus of the Vth Nerve (Fig. 10), but there are many normal cells.

The cells in the nuclei of the NN. IV (Fig. 10) and III (Fig. 11) are not quite normal, but they are less affected than the more distal nuclei.

D. *The large cells in the efferent nuclei in the higher parts of the central nervous system.*

1. In the cells of the nucleus DEITERS nearly all cells are swollen, but in the tracti DEITERO-spinales no degeneration was found.
2. In the nuclei coerulei the cells are swollen.
3. In the magno-cellular part of the nuclei rubri all cells are swollen in a high degree (Fig. 12) but without degeneration in the tracti rubro-spinales.
4. In the substantia nigra many cells have disappeared and those which are present are mostly swollen (Fig. 13).
5. In the nuclei subthalamici all cells have disappeared. Only a few have remained and they are very much changed, swollen (Fig. 14).
6. In the nucleus pallidus many cells have disappeared and the

remaining cells are swollen (Fig. 15). The ansa lenticularis has disappeared and also the bundle *h2* of FOREL.

7. All the large pyramidal cells and BETZ's cells are swollen in the gyrus centralis. BETZ's cells have disappeared in the gyrus paracentralis.

Most of the larger pyramidal cells in the third layer of the cortex in the frontal and parietal circonvolutions are swollen, without degeneration in the cortice-pontine systems in the pedunculus cerebri.

Resuming: we may conclude that in all the nuclei from which longer centrifugal fibres are sent out, the cells are very intensely damaged, and that the fibre-systems arising from those nuclei are sometimes but not always lost.

E. The unaltered grey matter containing normal cells.

The ventral nuclei pontis are unaltered. Neither were changes found in the three lateral nuclei of STILLING and the microcellular part of the red nucleus. All cell groups of the thalamus are normal. The same is found of the putamen, the nucleus caudatus, the claustrum and circonvolutions of the insula, the occipital and temporal lobe.

F. Summary of the localization of the altered cells.

There is known a disease of the nervous system called "Amaurotic idiocy". It is characterized by an interesting change of all the nervous cells. They are swollen, filled up with lipoids, the nucleus is pushed to the margin of the cell, with a rest of the tigroid surrounding it. Prof. Dr. BIELSCHOWSKY suggested that a metabolic constitutional lesion was at the bottom of this disease. Notwithstanding the changing of the cells, their axons are not necessarily affected and the fibres remain unchanged in amaurotic idiocy. Here in this heredo-ataxia we find the same changes which are found in amaurotic idiocy in many cells but not everywhere.

But in the described heredo-ataxia we find the typical cell-alterations in distinct cells, all confined to cells having a centrifugal signification.

They are localized in centrifugal cells.

This is true in regard of the

A. *cerebellum*. There is seen

1. all cells of PURKINJE are gone.
2. the cells in the *nuclei fastigii* are degenerated and swollen.
3. the same is seen in the cells of the *magnocellular part of the nuclei rubri*.
4. the cells in DEITERS' nuclei are also swollen and degenerated.

B. *striatum*. There is seen

1. most cells of the *nucleus pallidus* have disappeared, the remaining

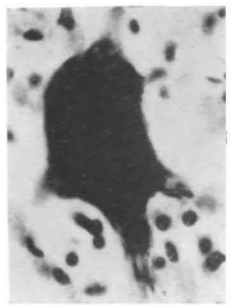


Fig. 6*a*. A normal cell of the ventral horn in the cervical intumescentia. (Cresylviolet.)

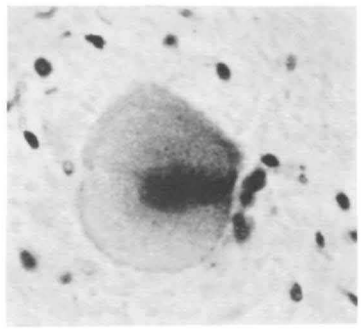


Fig. 6*b*. A swollen cell of the ventral horn in the cervical intumescentia of our case (Cresylviolet).

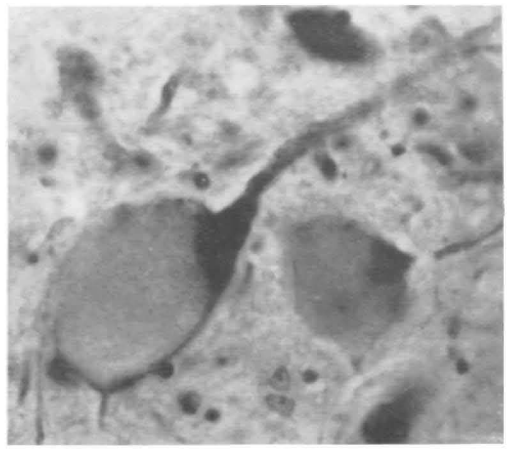


Fig. 7. Swollen cell in the nucleus Nervi XII. (Cresylviolet.)

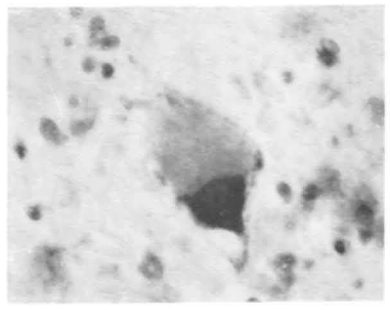


Fig. 8. Swollen cells in the nucleus Nervi VII. (Cresylviolet.)

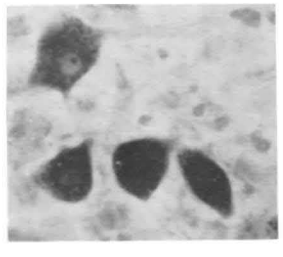


Fig. 9. Swollen cells in the nucleus Nervi VI. (Cresylviolet.)

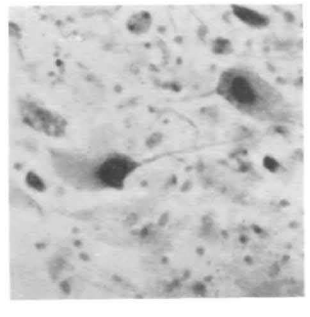


Fig. 10. Swollen cells in the nucleus motorius Nervi V. (Cresylviolet.)

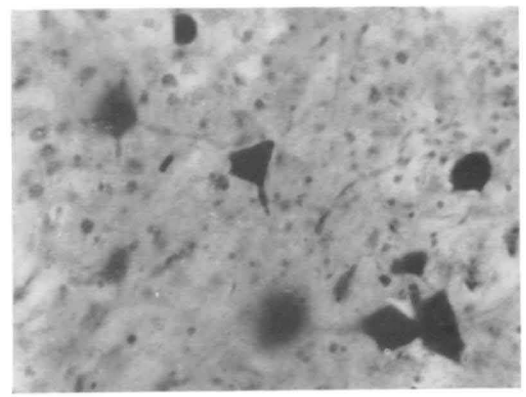


Fig. 11. Normal and swollen cells in the nucleus Nervi III. (Cresylviolet.)

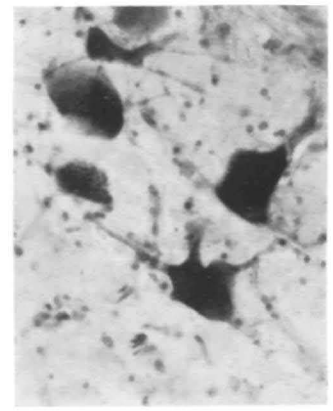


Fig. 12. Normal and swollen cells in the magnocellular nucleus ruber.

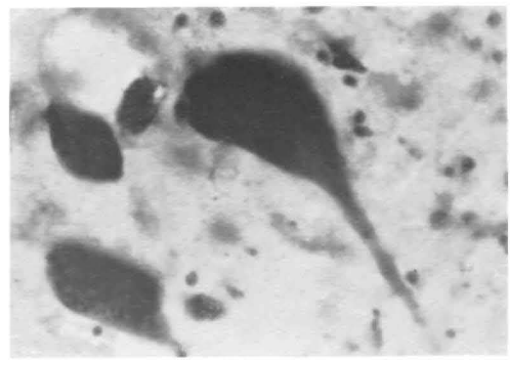


Fig. 13. Swollen cells in the Substantia nigra SÖMMERINGII. (Cresylviolet.)

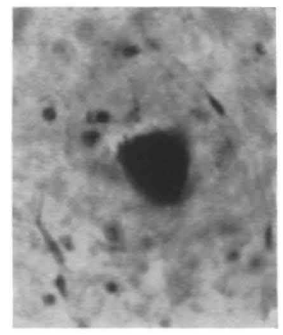


Fig. 14. Loss of cells an swelling of the remaining in the nucleus LUYS.

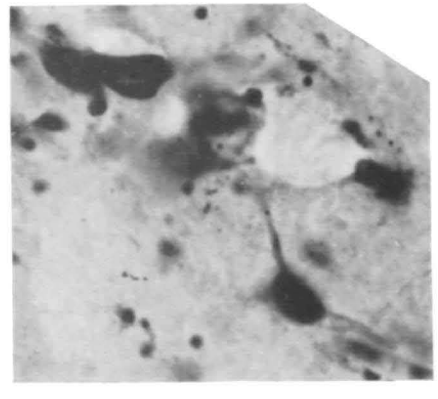


Fig. 15. Many swollen cells in the globus pallidus n. lentiformis. (Cresylviolet.)

ones are swollen. Together with the cell-alterations the ansa lenticularis and the bundle *h2* of FOREL are missing.

2. all cells of the *nuclei subthalami* are gone; the very few remaining cells are swollen.

3. the cells of the *substantia nigra* SÖMMERINGII are gone; those which remain, more than in the corpora LUYSI, are severely changed.

C. *Cortex cerebri.* In the frontal and parietal circonvolutions the large pyramidal cells have changed. In the paracentral circonvolutions BETZ's cells are gone; in the central ones the cells of BETZ as well as the large pyramidal cells in the third layer are swollen.

D. *The motor nuclei of the nerves above and in the medulla spinalis.*

The cells in the *oculomotor nuclei* of the pedunculus cerebri are only slightly changed. In the *pons and in the medulla oblongata* the cells of the motor nuclei are intensively swollen but only a few have disappeared. The change is strong in the nuclei NN. XII.

In the *medulla spinalis* the cells have nearly all disappeared. In *the cervical intumescentia* still exceptionally a normal cell may be found, most of them have disappeared and the remaining ones are swollen. In the *thoracic part, the lumbar intumescentia* and in the *sacral medulla* all motor cells have disappeared.

Now summarizing: we find a relatively sharp localization. Only cells, sending fibres in a centrifugal direction, have been damaged or disappeared.

CONCLUSIONS.

Much has changed, since FRIEDREICH, as the first, in different articles in VIRCHOW's Archives (1861—1867) published the history of atactic children in the same family. His work created a new disease, called "Tabes of FRIEDREICH". It was accepted in his days that at the bottom of this disease was a defective predisposition of the dorsal and lateral funiculi in the medulla spinalis.

Gradually it was recognized that in this atactic and family disease the cerebellum also could be damaged and the possibility was defended that this organ could play a part in its pathology. In 1893 PIERRE MARIE published a series of atactic sufferers, no longer children, but adults of the same family. He called his disease "heredo-cerebellar ataxia". The Tabes of FRIEDREICH and the illness of MARIE seemed to have a certain relation to each other. Soon tendencies appeared to bring them together as diseases with many points of similarity. The hodologic conceptions of that time account for the fact that the suffering of the dorsal and lateral cords in the medulla made it possible to understand its pathology.

In 1891 WARREN TAY and in 1896 SACHS described another family disease, found in very young and mostly Jewish children, which they called "Amaurotic idiocy".

Those children, after having shown blindness and idiocy, died before they were a year old. The pathology of the brain in these children was characterized by a grave degeneration of all the nervous cells.

They were swollen, the nucleus with part of the tigroid was forced to leave the centre of the cell and was pushed to its margin. But, together with the damage of the cells, there existed no visible degeneration of the fibres issuing from them. In this way the usurpation of hodology in pathology was broken.

Soon afterwards SPIELMEYER and VOGT described a family disease, identical to the amaurotic idiocy of WARREN TAY-SACHS and a nearly similar pathology, in older children. And now the question arose if the pathology of heredo-ataxia could not be placed on the same level with amaurotic idiocy. Often, not only in the case here described, cell changes were found in heredo-ataxia. In amaurotic idiocy cell-degeneration was found without fibre degeneration. In heredo-ataxia often systematic fibre degeneration was found but now the necessity occurs to ascertain if perhaps in such cases also cells were found in degeneration. Hodology alone seemed no longer sufficient.

As we have seen before, it was Prof. BIELSCHOWSKY who first suggested the idea that amaurotic idiocy should be a constitutional change in the metabolism.

This idea may be transferred to such cases as those here described.

It is true, the cell-changes in the described case were identical to these in amaurotic idiocy, with the restriction, however, that they had a distinct localization. They were only found in cells, whose axons formed *long centrifugal* systems. Such a localization may be in accordance with the idea of the metabolic constitutional factor, if we accept another hypothesis, that there exists, in such cases of heredo-ataxia, an insufficiency of all cells from which centrifugal systems originate. But, still there will be required many researches in family diseases, as well as in those where progressive dementia is combined with grave choreo-athetosic movements, and compared with cases where only disturbances in motility exist and with cases where the progressive dementia is combined with optic atrophy. Perhaps any general conception might be defended at that time.

It will be necessary to extend this research to the various other organs of the body and perhaps it will be possible to accept the hypothesis that also in heredo-ataxia the constitutional insufficiency of the centrifugal systems is at the bottom of the disease.