Central nervous system

The congenital disorders of the central nervous system were a prominent subject on the pages of the preceding chapters. There is no sharp line of demarcation between the symptoms of the innate lesions of the central nervous system and those acquired in early infancy. Extensive experience from 30 years of work in clinic and practice is available under the collective term «brain damage of early infancy» on the innate diseases and those acquired in babyhood and early infancy.

In this connection, the studies of many years by G. DESTUNIS (1957–1960), G. DESTUNIS and E. SCHMIDT (1956), on encephalopathy and debilities of various genesis deserve to be mentioned. The authors worked chiefly on implantations of diencephalon. More reports in this field are available by R. JAKOBS (1960); H. GOLDSTEIN (1961); J. M. DAVID and DAVID, E. A. de AURELIA (1960); P. E. DELONS and J. COUGOULE (1959); W. ZELLER (1957); H. FELDMAN (1961, 1979, 1982). The voluminous literature of DOWN's syndrome is mentioned in a special chapter.

The following diseases have been picked out from neurology and psychiatry; decisive for this selection were the viewpoints of clinical importance and experience in the field of cell therapy.

Infantile cerebral paresis

The forms of infantile cerebral paresis have been outlined in the chapters of «Mental and multiple physical disability». The following survey is just another

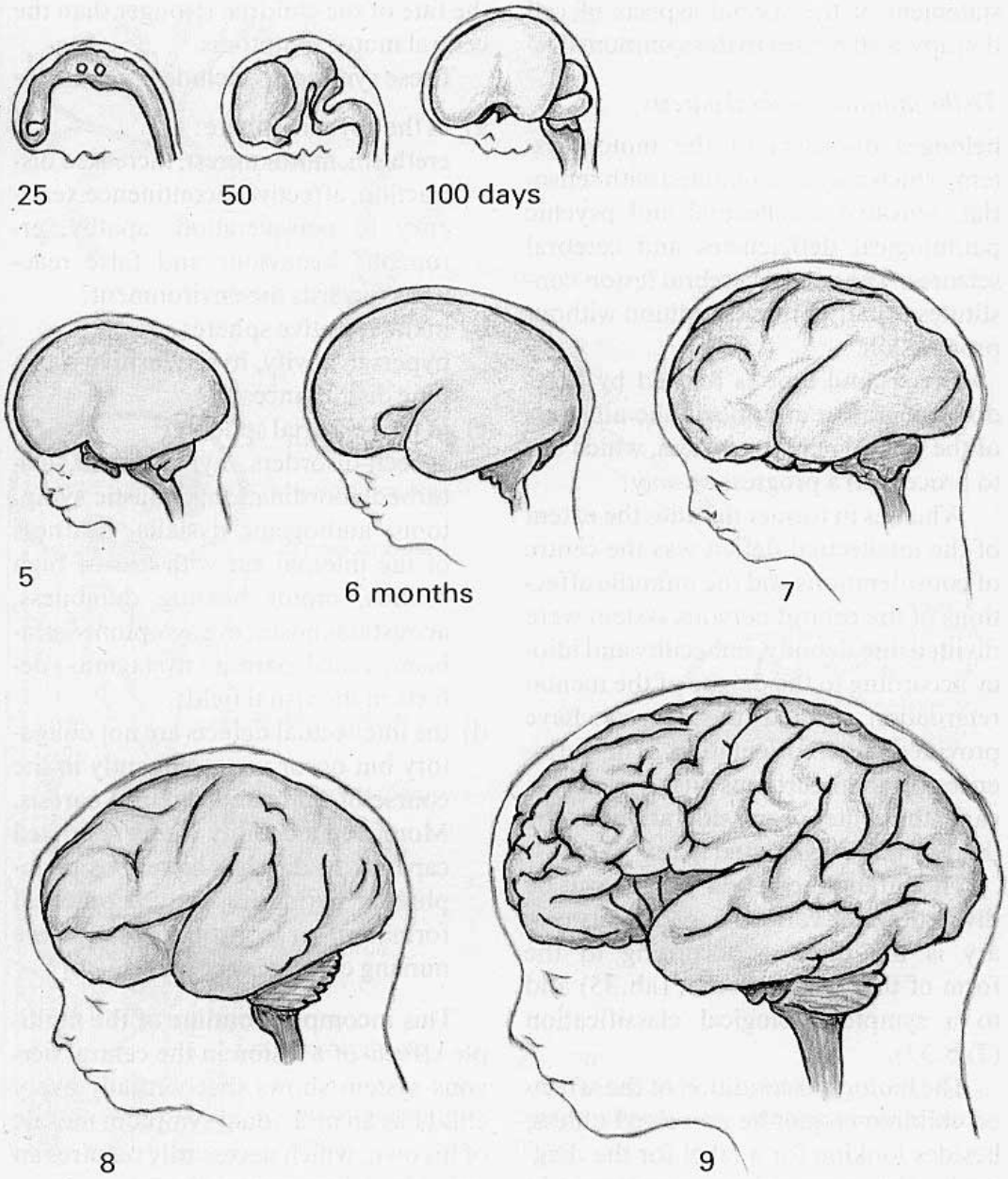


Fig. 268:
Embryonal and fetal development of human brain in days (100) and months (till 9).

statement of the special aspects of cell therapy with regard to the symptoms:

To the infantile cerebral paresis

belonges disorders of the motor system, which may be combined with sensorial, sensitive, intellectual and psychic pathological deficiencies and cerebral seizures. The causal cerebral lesion constitutes usually a final condition without progression.

The second type is formed by heredodegenerative and metabolic ailments of the central nervous system, which use to proceed in a progressive way:

Whereas in former decades the extent of the intellectual deficit was the centre of considerations and the infantile affections of the central nervous system were divided into debility, imbecility and idiocy according to the degree of the mental retardation, specially the last years have provided other orientation. The influences on the neuromuscular system became the center of considerations as the therapy may be initiated here.

The infantile cerebral paresis can be divided under various aspects; customary is the division according to the form of the motor effects (Tab. 35) and to a symptomatological classification (Tab. 32).

The biological condition of the affected children cannot be perceived unless, besides looking for a label for the diagnosis, the concomitant symptoms in other fields – in addition to the motor effects – are taken into account. This helps to understand the pathobiological influences of the basic process on the child's individuality. Apart from the central neuromuscular symptoms manifesting themselves by spasm, hypotonea, chorea, dyskinesia and ataxia, a wide variety of concomitant symptoms is found in the sensorial, sensitive, psychic, intellectual and somatic spheres; they may influence the fate of the children stronger than the central motor symptoms.

These symptoms include:

a) in the psychic sphere:
erethism, motor unrest, increased distraction, affective incontinence, tendency to perseveration, apathy, erroneous behaviour and false reactions towards the environment;
b) in the sensitive sphere:
hypersensitivity, hyposensitivity, trophic disturbances;
c) in the sensorial sphere:
speech-disorders, hyperkinesia, disturbed coordination, acoustic symptoms, audiogenic dyslalia, deafness of the internal ear with loss of high sounds, motor hearing dumbness, acoustic acnosia; eye symptoms, strabism, visual paresis, nystagmus, defects in the visual field;
d) the intellectual defects are not obligatory but occur very frequently in the course of untreated cerebral paresis. Moreover, a debility with a restricted capacity to develop or serious oligophrenia permitting only a practical formation or constituting a «mere nursing case» may come on.

This incomplete outline of the multiple effects of a lesion in the central nervous system shows that virtually every child has an individual symptom mosaic of his own, which necessarily requires an individual therapeutic scheme.

Residual therapy

In cases of serious multiple disability and if cerebral paresis is taken up in late periods (beyond the second year of age), the causal and symptomatic measures mentioned above are frequently insufficient to provide decisive progress because the lesion in the central nervous system is too deep. Both the callisthenics and the paedagogical measures require a

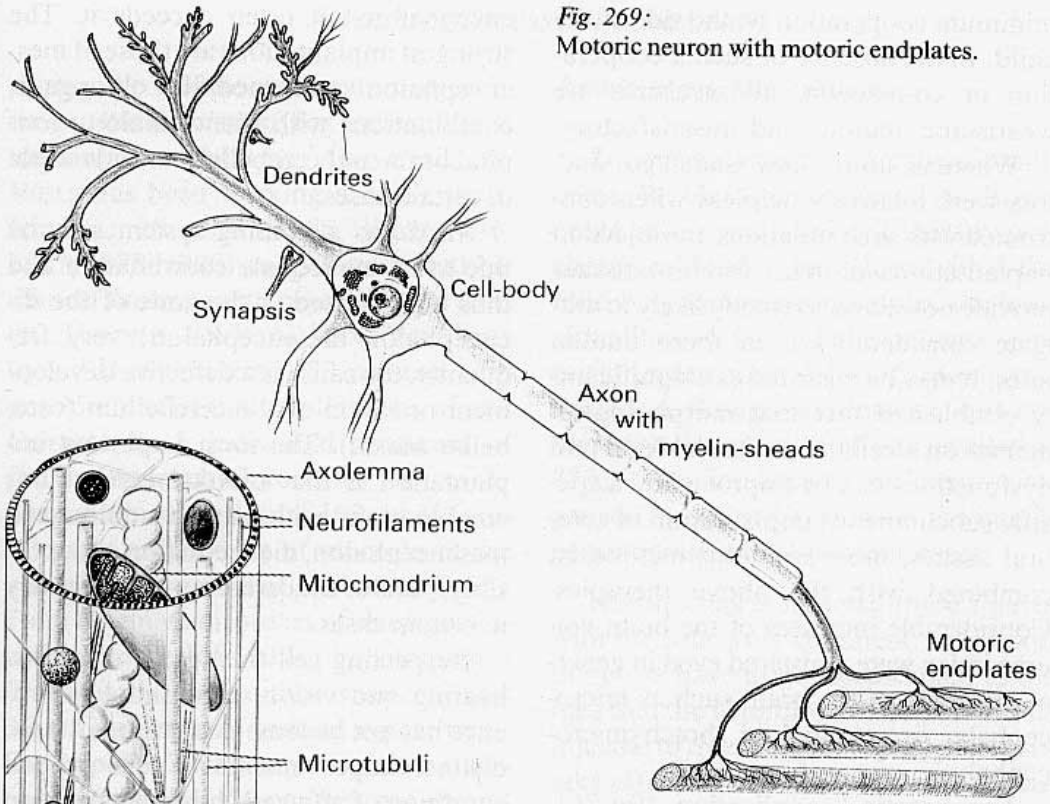


Fig. 269:
Motoric neuron with motoric endplates.

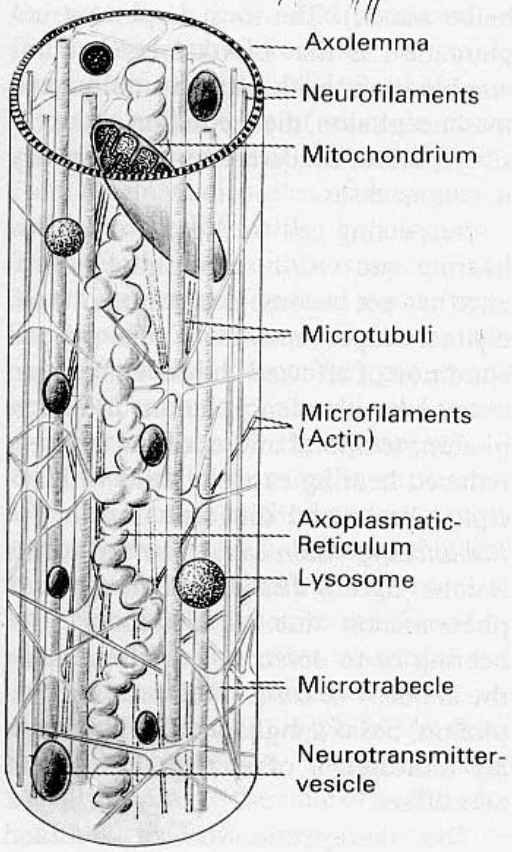


Fig. 270:
Substructure of an Axon with the – for the metabolite-transport – important subcellular structures.

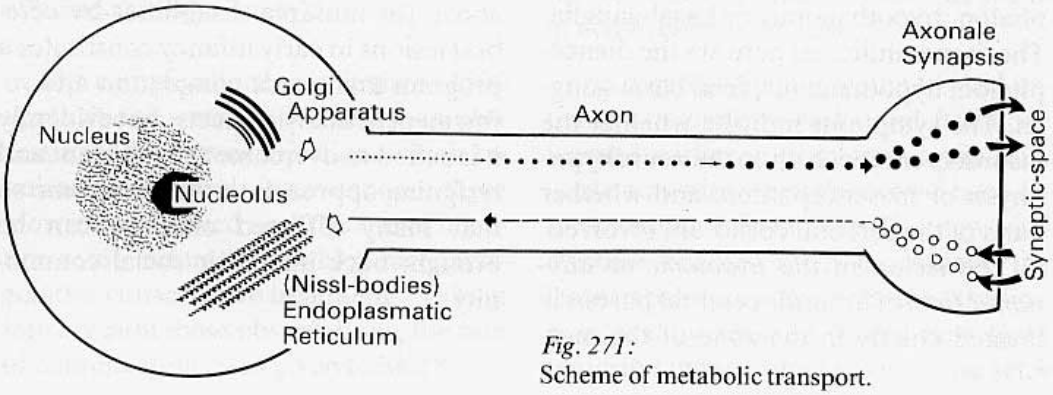


Fig. 271:
Scheme of metabolic transport.

minimum cooperation on the side of the child. In the absence of such a cooperation or co-reaction, all measures are wearisome, tedious and unsatisfactory.

Whereas, until a few years ago, doctors were relatively helpless when confronted with such situations, the injection implantations of fetal cerebral tissues provide nowadays a remedy likely to mitigate considerably even these human fates. It may be regarded as a significantly established fact that morphological defects on a cellular or tissular level and dysfunctions can be improved by a specific subcutaneous implantation of cerebral tissues, more so if this method ist combined with the above therapies. Considerable increases of the brain volume index were registered even in general disorders of the brain such as microcephaly or mongoloid brachymicrocephaly.

For practical application (fig. 261, 262) the following remarks must be taken into consideration: *spastic forms* are as a rule, exclusively or prevailingly, lesions of the cortex. Implantation tissues are available as cerebral cortex, cerebral hemisphere or, in localized cortical atrophy, as frontal, temporal, parietal, occipital brain. The effects on the movements are modest beyond the 3rd year of age.

In the *types of choreo-athetosis*, the lesion by nuclear icterus or early infantile encephalitis is in the zones of the diencephalon, hypothalamus or basal-ganglia. The tissues indicates here are the diencephalon, hypothalamus, fetal basal-ganglia. The symptoms indicate whether the disorders encroach upon the neurohypophysis or mesencephalon, and whether parts of the cerebral cortex are involved.

The lesion in the *hypotonic* or *adynamic form* of infantile cerebral paresis is located chiefly in the zone of the mesencephalon but often exceeds it. The strongest implantations are those of mesencephalon and medulla oblongata; combinations with diencephalon, occipital brain and cerebellum are advisable in certain cases.

Ataxia as a guiding system may be due to an inadequate coordination and thus be localized in the zone of the diencephalon/mesencephalon; very frequently, the cause is a defective development or lesion of the cerebellum (cerebellar ataxia). The most important implantation is that of fetal cerebellum; combinations with medulla oblongata, mesencephalon, diencephalon and, possibly, parts of the cerebrum are necessary in certain cases.

Respecting cell therapy in disturbed hearing and vision, substantial experience has not become known so far. Still, distinct improvements of the general condition of affected children have been obtained with diencephalon, mesencephalon, temporal and occipital brain in reduced hearing capacity, and with occipital brain and diencephalon in *disturbances of vision* caused by the cortex lesions. *Speech disorders* are a complex phenomenon due to disturbances of hearing or to defective coordination in the majority of cases. Tests with diencephalon, basal ganglia and frontal brain are indicated if other remedies cannot take effect.

The therapeutic scheme outlined above for multiple disabilities by cerebral lesions in early infancy constitutes a program that needs completion and refinement in many respects; but evidently it is suited to overcome the reluctant and resigning approach to this syndrome so that many afflicted children can be brought back into their social community.

during the middle and mature age belong to the most satisfying indications of implantation therapy. Above all, N. WOLF has been working at these problems for 20 years (1966, 1969, 1976, 1977, 1978, 1980) and substantiated his clinical findings with psychological tests (W. HENNIG, 1969). N. WOLF's patients included at that time 133 persons who got 2500 individual applications of cell therapy. Each individual treatment of the brain-atrophic processes was an intramuscular injection of 100 mg of frontal brain and 150 mg of placenta of the same sex. A number of patients suffering from obstinate disorders of sleep got additional doses of 100 mg hypothalamus lyophilisate. Unlike the usual cell-therapeutic practice of putting repeat treatments off to a term beyond a time interval of 6 months, 66 patients got several repeat treatments at intervals of 4 weeks in order to intensify the therapeutic effect. Thanks to favourable experience with this intense method and as complications are rare, it is believed that cell therapy of the brain-atrophic processes of the middle and mature age should be started with a intensive treatment i. e. 3–4 treatments as described above are aplied at intervals of 4 weeks. As these initial concentrated therapies have usually improved the state of health considerably, the further applications can be effected at longer intervals.

The complications seen in those 2500 applications were, in two cases, an abscess near the site of injection, which required a surgical intervention; three more cases showed near the site of injection some indurations, which regenerated after conservative treatments. Taking into account these observations, the rate of complications was given to be 2%.

Results of psychological tests

To substantiate the therapeutic outcome, W. HENNIG conducted on 40 patients before and after cell therapy psychological studies, which provided the following summarizing results: the individualities of 50% of the patients were revitalized to normal. In 37% also a revitalization, though less intense, was observed so that positive effects resulted in 87%. The intellectual efficiency improved by about 10 points of the intelligence quotient in 60% of the cases.

HENNIG has completed these figures with the following comment: «One will therefore have to get accustomed to the idea that the heterologous implantations injected to treat brain-atrophic processes take effect on various types of individuality and efficiency, according to the degree and localization of the preceding lesions. Moreover, one cannot ignore the problems resulting from the cognition that, possibly, the brain-atrophic processes do not stop in certain cases, that the disintegration continues, that the intellectual efficiency goes on weakening and that, nevertheless, the patient's vitality, physical efficiency, humour, confidence, sociability and interest appear normal after the treatments. The aspect of vitality makes these patients look healthy and efficient but their intellectual achievements decrease.

As regards sociability, the treated patients can perform tasks and functions learned earlier and achieve again adequate activities when they come back into their old environment. The new vital impulse enables them to achieve the learned behaviour and activities; the limit is usually reached where new tasks requiring independent solution are set.»

Heredodegenerative diseases

In view of the many causes and forms of heredodegenerative diseases of the central nervous system, the question as to whether or not cell therapy shall be applied deserves critical considerations; one is often confronted with the alternative whether an enzyme defect or an autoaggressive destruction of tissue is the cause of the pathological process.

Empirism justifies the ambivalent recommendation to try a therapy with placenta, liver (possibly adrenal gland) because individual observations delay not only the regressive symptoms but also the progress of development. The ambivalence of this trial appears from the fact that cerebral tissue, especially cerebral marrow, is not effective, often entails febrile reactions. Tissue of the white substance, therefore, should not be administered even if just a trace of an autoaggressive tissular process is detected.

Generally, the existing products are not qualified enough to meet the requirements for a treatment of degenerative processes in the central nervous system (Tab. 22). Concentrates of lysosomes and mitochondria are more promising as a more specific use of the cell organelles in question is necessary.

A considerable progress is to expect in this field in the next future.

Degenerative Disorders of the cerebral white matter

It is generally accepted that the course of the majority of degenerative disorders of the central and peripheral nervous system cannot be manipulated by therapy. This view is further supported by the frequently used adjective «heredodegenerative». However, specific observations of a number of different degenerative manifestations in the white cerebral matter (myelin degeneration of the brain and spine) do not confirm the validity of a specific treatment strategy, unless long-termd results gained from a sufficiently large group of observed patients is available.

Nevertheless these individual observations revealed some very striking regeneration features even during the first week and months following the onset of the treatment and they impel us to offer all victims afflicted with this desease not only a diagnostical label, but actual medical help. The discrepancy between the diagnostic display accompanied by various unpleasant annoyances and the therapeutic nihilism produces a red thread which runs through the anamneses of many patients.

Myelin, the predominant component of the cerebral white matter, consists of proteolipid layers surrounding the axons of the nerve cells. While the myelination – as a postponed fetal process – occurs in the first years of postnatal life, the deficiencies of the «marrow-sheat-formation» also starts in the first years of life. This white substance is in an immature state at birth. Even though all cerebral cells are present at birth and no fresh ones appear at a later stage, the brain is the only organ which is not in a position to ensure the sustaining of life independently at this stage. Life sustenance can only be assured by the age of 4 years when the secondary structures (dentrides, synapses, axones, glia) are fully matured and insulation of the nerve fibre conductors with the aid of Myelin (medullary sheath) is complete.

Since the maturing of the medullary sheath (myelinisation), which is in fact a delated fetal process, takes place during

the first years of life and is only completed by age 4, initial defects in the maturing of the medullary sheath initially begins during the early years of life. Depending on the actual time at which they appear, we differentiate between the more serious generalised «de-medullisation disorders» which occur at a young age as a result of an insufficient «myelinisation», and the more localised manifestations occurring in older age groups which indicate a «myelin-degeneration».

Somewhere in between we have extensive, but not generalised degenerations which occur in the middle decades of life, such as in Friedreich's ataxia (this disease occurs most frequently between the ages of 10 and 30), or else multiple sclerosis (disseminated sclerosis = scattered focal substitution of nerve tissue by connective tissue), most frequently occurring between the ages of 20 and 40.

Depending on age and localisation we are faced with a broad spectrum of syndromes (= diagnoses) and in specific cases it can be quite difficult to match an individual collection of symptoms with any specific diagnosis. The most important diseases categories are listed below:

Leukodystrophies
Metachromatic leukodystrophy (sulfatide lipidosis)
*Globoid leukodystrophy (*KRABBE *disease, cerebrosid lipidosis)*
*Spongy degeneration of cerebral white matter (*CANAVAN *disease)*
*Sudanophilic leukodystrophies (*PELIZEUS-MERZBACHER *disease)*

Demyelinating diseases
*Diffuse sclerosis (*SCHILDER *disease)*
Disseminated sclerosis (Multiple sclerosis)
*Neuromyelitis optica (*DEVIC *disease)*

Cerebro-occular degenerations
Amaurotic idiocy – infantile variety (TAY – SACHS);
Late infantile variety (BIELSCHOWSKY);
Juvenile variety (SPIELMEYER – VOGT);
Tapeto-retinal degeneration.

Spinocerebellar degenerations
*Syndrome cataracte-oligophrénie et ataxie spinocerebelleuse (*MARINESCO-SJÖGREN*-syndrome)*
*Congenital ataxia, aniridia, mental retardation (*GILLESPIE*-syndrome)*
CHARLEVOIX-SAGUENAY*-syndrome*
TROYER*-syndrome*
*Ataxia teleangiectatica (*LOUIS BAR *syndrome)*
FRIEDREICH*s ataxia*
Refsum' disease
Abetalipoproteinemia (Acanthosis; BASSEN-KORNZWEIG*-syndrome)*
Recessive ROUSSY-LEVY *syndrome*
Recessive type II OPCA *(*FICKLER-WINKLER *type).*
*Myoklonus-encephalopathy in children (*KINSBOURNE*-syndrome)*

Cerebro-cutaneous degenerations
Tuberous cerebral sclerosis (BOURNEVILLE);
Neuro-fibromatosis (von RECKLINGHAUSEN);
Angiomatosis retinae et cerebelli (V. HIPPEL – LINDAU).

Spino neuromuscular degenerations
Neural muscular atrophies
(WOLFARTH – KUGELBERG – WELANDER; WERDIG – HOFFMANN; CHARCOT – MARIE – TOOTH – HOFFMANN; DEJERINE – SOTTAS);
Progressive muscular atrophies
(DUCHENNE; Erb);
Myatonia congenita (OPPENHEIM);
Myatonia (THOMSEN);
Karnithin myopathia
Myasthenia gravis (ERB – GOLDFLAM);
Amyotrophous lateral sclerosis (CHARCOT *syndrome);*
Syringomyelia.

Degenerations of the basal ganglia
*Hepatolenticular degeneration (*WILSON *disease)*
Dystonia musculorum deformans (Torsions-dystonia)
HUNTINGTON*-chorea*
PARKINSON*s disease*

Friedreichs Ataxia

Beside the multiple sclerosis the Friedreich ataxia is the most important disease in the heredodegenerative disorders of the central nervous system. The common onset is the late childhood or adolescence. The clinical symptoms are correlated to a progressive cerebellar and spinal cord degeneration and dysfunction. Their base ist a degeneration of the posterior column of spinocerebellar and corticospinal tracs. The main symptoms are:

gait disturbance,
incoordination of upper limbs and speech-motoric,
highly arched foot (caved foot),
hammer toes,
scoliosis,
cardiomegaly (following necrosis of cardiac muscle fibers).

A treatment of this recessive-autosomal disease seemed to be impossible till now and is therefore denied.

By treating a number of cases with degenerative diseases of the central nervous system for the last years, the *Friedreich'sche Ataxia* has only been included recently. So far we have only experience with a few cases, and at this time it is not possible to give a definite judgment on the longterm effect of the treatment. It is remarkable that in these single cases not only a stagnation of the illness could be obtained, but also a restoration of the impaired functions could be registered.

Multiple sclerosis

is caused by a myeline degeneration which presents clinical symptoms most often between the ages of 20 and 40. The most predominant features are impairment of walking, speech and eye-sight as well as numerous neurological outfall symptoms. Periods of progression, remission and even improvements create a mercurial pattern, at the end of which there is usually complete invalidity.

The method of treatment applied now, has not yet been published. The first publications can only be expected when we can look back on an experience of at least two years. Earlier experiences with implantations of fetal muscle of the spinal medulla and tissues of the central nervous system did not bring about a convincing progress, so that the treatment was changed. The basis for this were individual observances. The total concept of the method of treatment, as summarized thereafter, has probably still not reached its optimum result.

Disposition – exposition

Many of the degenerative diseases are hereditary in an autosomal-recessive manner, whereby the pervasiveness of Friedreich's ataxia is particularly great. This hereditary factor very often results in therapeutic resignation. However, in order for a disease to occur on the basis of a hereditary disposition, several *realisation factors,* i. e. additional influences, must be present, which turn the existing faulty disposition into a functional disturbance which ultimately results in disease symptoms. In the context of heredodegeneration of the central nervous system with reference to the interaction between hereditary disposition and the environmental influences which acts as a trigger, the following guidelines can be provided:

1. *Disability caused by predisposition (constitutional)*
   a) of the intestinal resorption and digestive organs;
   b) lysosomalic defects (insufficient production of secretions of lysosomalic enzymes).
2. *Strains produced by environmental factors (expositional)*

which trigger the outbreak of the illness on account of the constitutional weakness. These include:

c) strains caused by de-naturalized foods which cannot be properly broken down, because the inadequate organism lacks the appropriate enzymes;
d) viral illnesses (measles, viral encephalitis, herpes infections and others);
e) immunisations;
f) gastro-entero-colitis with necroses of the intestinal resorption areas.

From the statistical point of view it is practically impossible to evaluate the significance of hereditary predisposition versus triggering factors. On the one hand a family, in which several siblings are afflicted would appear to indicate a dominant influence of hereditary factors, but on the other hand, these members of the same family will have been exposed to the same environmental and nutritive conditions. Even studies on the frequency of distribution in specific geographical areas do not provide an unequivocal answer. Upon discovering that multiple sclerosis occurs 5 × more frequently in the north of England (Orkney Islands) compared with Holland, and 20 × more frequent than in the South of Europe (South of France), then one would be inclined to attribute this to a racial predisposition. In the mixed population of Eastern Canada (Ontario, Quebec) which consists of people of English, Irish, Frenchs, Italian and German descent, the incidence of degenerative diseases of the central nervous system in relation to the population size is probably the highest in the entire world. Thus the significance of the racial factors (predisposition) is put into perspective.

The most convincing arguments regarding the amount of influence exercised by environmental factors are provided by cases occurring in early childhood, in which children of normal development suddenly display symptoms indicating a degeneration of the white cerebral matter following measles, whooping cough, immunisations, herpes infections, entero-colitis and undefined infections.

Cerebral metabolism and nutrition

Studies on the relationship between nutrition and brain development have revealed that the rate of maturity and of intellectual development is adversely affected in the presence of nutrition which is either overall deficient or deficient in protein in the course of the first 3 years. (Summary F. SCHMID, 1981). Much less attention has been paid to the correlation between disorders of the brain and diseases of the digestive tract. Chronic constipation which is not helped by laxatives, which accompanies severe cerebral pareses and degenerative afflictions, and the flatulent spasms following food intake as well as severe anatomical and functional changes in the upper digestive tract (ulcers, scars, mucosal atrophies) which are often quite severe, are frequently regarded as unavoidable consequences of brain diseases (FEHL). The presence of dystrophy with sufficient food intake is also considered to be momentous.

Only upon the discovery of neurohormones (peptides) which are formed in the intestines and in the brain and which include neurotensin, cholecystokinetic-like peptide, somatostatin, VIP (vaso-active intestinal polypeptide and others) SCHMID, F. (1981), it becomes possible to recognize and evaluate the relationship as no longer being a one-way street from brain to intestine, but to view it in the context of its mutual dependency.

The worldwide efforts directed at find-

ing a cure for multiple sclerosis and Friedreich's ataxia have resulted in a number of informative details:

A. BARBEAU's working team (1979, 1980) in Montreal discovered a faulty fatty acid composition (lack of linoleic acid 18:2) of the cholesterol esters in the HDL (high density lipoproteins); they indicated a deficient incorporation of the linoleic acid into the surface phosphaditylic choline of the chylomicrones. Due to an overloading with defective cholesterol esters, there occurs a difficiency of usable lipo protein components which are required for the synthesis of myelin. Secondary consequences are: insufficient activation of the enzyme lipoamid-dehydrogenase (LAD), of the pyruvate-dehydrogenase complex, slow pyruvate oxydation, glucose intolerance, insufficient production of acetyl choline, as well as a drop in the glutamine and asparaginic acid level in the blood.

These intermediary metabolic changes were emphasized by the P. KARK (1976, 1982) working team in Los Angeles.

Parallel to this metabolic lapse which is caused by the mucous membrane of the small intestine, phosphatidyl choline molecules with an abnormal structures can be incorporated into the cell membranes, resulting in disturbances in the calcium-magnesium-taurin interchange and thus leading to a faulty myelinisation. Other reasons include a delay in the absorption of the glucose into the cell, a reduction in the pyruvate oxydation and the presence of diabetic metabolic problems. The linoleic acid deficiency (phospholipids, cardiolipin), particularly when it is located at the interior membrane of the mitochondria, can produce a «mitochondrial energy deprivation», resulting in symptoms such as muscle weakness, scoliosis and cardiomyopathy.

These findings observed in connection with Friedreich's ataxia can also be indications of other CNS-degenerations. Numerous tests on multiple sclerosis cases have revealed an abnormal myelin composition not only in the demyelinised areas, but also in the less obvious tissue parts. (GERSTL, R. B. et al. 1965; BAKER, R. W. R. 1963; CUMINGS, J. M. 1953). SUZUKI, K. et al. 1973; RIEKKINEN, P. J. and CLAUSEN, J. 1969 discovered myelin reductions of healthy parts in about 25–30% of cases.

In spongy degeneration of the central nervous system (CANAVAN-syndrome, V. BOGAERT) gigantic, abnormal mitochondrias with dense, filamentous matrices are present, and also distorted deformed cristae (BANKER, B. Q., et al. 1964), which are entirely in keeping with the hypothesis of Friedreich's ataxia.

These findings, which are somewhat contradictory, are very strong indicators of enzyme defects, whereby many arguments point in favour of a central position of the intestinal food intake and digestion. L. GILKA (1973, 1975) pointed out this correlation. The successes achieved by H. T. R. MOUNT (1973) in treating patients suffering from multiple sclerosis with vitamin B_1 liver extracts and special diets further substantiate this theory.

Treatment strategy

The abundant availability of statistical, biochemical and clinical data can be joined in a network with a firm knot – but with many gaps. Nevertheless, the present stage of acquired knowledge justifies the concept of commencing active therapy in all cases, where

a) deviations in the metabolism are recognized and
b) therapeutic aids are available for treatment.

Based on the expounded strategy, the treatment is based on three columns:

1. Nutrition (diet);
2. Enzyme substitution;
3. Regeneration of the cell functions.

Nutrition and diet

Over the last 3 generations the basis for nutrition under the categories foodstuffs – nutrients – luxury foods has increasingly veered towards the nutrients and luxury foods in most of the industrial nations. Preparation, preservation, colouring and packaging all serve purposes quite removed from nutrition. The preoccupation with calories and protein percentages, carbohydrates and fats in conjunction with the processes required to maintain the foods in a «sterile» condition, have resulted in converting most of the foods (containing «live» ingredients) into pure nutrients (energy suppliers). The essential components required for the synthesis and decomposition of a nutrient product, the so-called ferments (enzymes), are lost at temperatures as low as 45–60° C. These enzymes, which are contained in the «foodstuffs» are effective aids in the nutritional decomposition of the foods in the digestive tract. The de-naturalization of the foods and the destruction of its ferments have resulted in the fact that fresh foods are almost unavailable in certain geographical regions and in areas of industrial concentration, and that all nutrition leans heavily towards canned nutrient ingredients and luxury foods. Thus the organism is expected to cope with a double burden: By eliminating the ferments and natural ingredients (such as minerals, trace elements), the natural assistance required for the decomposition of food is removed, but at the same time the de-naturalization of the nutrients as present in canned foods, puts a burden on the organism by expecting it to digest and decompose nutrients, without being equipped with the enzyme apparatus to cope with this on its own.

Thus the increased incidence of degenerative diseases in the congested areas of North America, England, Ireland and the Orkney Islands, but also the extreme frequency of intestinal cancer observed in Iceland, is more likely to be due to environmental influences (dry meat, canned foods, insufficient supply of fresh food) than to ethnic factors.

Translated into the field of practical nutrition, the following guidelines are recommended:

The distribution of food intake should be geared towards *«foodstuffs, whilst reducing de-naturalized nutrients and especially luxury foods.»* To achieve this, the following are considered most suitable:

First course consisting of unpreserved, well-ripened fruit or fruit juices: Papaya, mango fruit, pineapple, melons, figs, pears, apples, peaches, apricots, berry varieties in season.

The ferments contained in these fruits will assist in the decomposition of the subsequent main course.

The *main courses* should be low in animal protein and refined carbohydrates (white sugar, white flours, pastries made from white flours). Animal protein should be derived from fresh white meat (veal, fish, chicken, turkey), whereas red and preserved meat should be avoided as far as possible. An exception can be made in serving small quantities of raw liver, spleen or high-quality raw beef mince on salad-diet days. The anamneses of most of the patients revealed that they instinctively removed all fat meat from their nutrition and for this reason pickled, grilled and smoked meats should be left out altogether.

Milk and egg dishes are suitable sources of protein, whereby the milk should be taken in its natural state and the eggs

preferably uncooked (beaten or mixed with fruit juices).

The fat intake should be limited to vegetable fats, and fats of animal origin are to be eliminated. The best sources highly unsaturated fatty acids are the following:

Sunflower oil, soya oil, nuts and nut oil. The only known sources of the prestage of linoleic acid (gamma-linoleic-acid) is breast milk and Primerose oil. A linoleic acid preparation which is available in Canada is EFAMOL. Lard and denaturized protein fat complexes should be avoided.

It is most important to avoid canned, de-naturized, coloured, bleached foods and foods to which volume expanders have been added, as much as possible. On or two salad-days with small helpings of milk, cheeses and egg dishes will play an essential role in activating the digestive organs.

Enzyme substitution

As long as the causal enzyme defects in specific degenerative diseases are not known, a broad-spectrum regime of enzyme substitution is recommended during main meals. The enzyme preparations enhance the natural nutrition value of the food and replace it whenever it is not possible to maintain a consistent diet of undenaturized foods. The preparations should contain ferments which decompose fats, proteins and celluloses. The following are recommended:

Wobenzym tablets,
2 × 2 to 3 × 3 daily as a source of vegetable and bacterial enzymes;

Vitafestal,
3 × 1 coated tablets, daily as a combination of digestive ferments, vitamins and trace elements;

Bilicombin,
2 × 1 coated tablets daily as a fat-decomposing enzyme preparation;

Panpur, Panzynorm
at a dosage of 2–3 coated tablets daily, are also suitable ferment combinations.

Wobenzym may be combined with any one of the above-named preparations. A suitable preparation which is available in Canada is Enzyme Digest. It contains Betaine HCL, Papain, Bromelein and Mycozyme.

The efficacy of the dietetic measures can be increased by the administration of intravenous injections of vitamin B_1 (100 mg/ml), B_{12} (1000 mcg/ml) and raw liver extract such as Reticulogen/ Lilly, as well as Efamol as a source of linoleic acid. At present we do not have any experience with European liver extract preparations as applicable to this field.

Regeneration of the cell functions

In most cases of regenerative disease, cellular metabolic disorders are present in varying degrees, starting from the intestinal mucous cells up to the final segment forming part of the process, the nerve cells. Experiments carried out in the past, when fetal brain tissue was used in an effort to influence the disease, have brought no convincing results. Only the inclusion of the initial elements of the metabolism have lead to a significant breakthrough in this field.

The regeneration of the digestive organs can be approached from two angles:

a) By injection implantations of

fetal small intestine	100 mg;
fetal duodenum	100 mg;
fetal liver	150 mg;
pancreas	100 mg;
placenta, according to sex	150 mg;
suprarenal gland, according to sex	100 mg.

These implantations of lyophilisates

should be administered subcutaneously at 6-monthly intervals and usually result in a specific improvement whithin several days. Quite often the peripheral blood circulation is improved after only a few hours. In cases of marked ataxia the combination of fetal cerebellum (100 mg) is recommended and for persistent constipation a combination of lyophilisied colon (100 mg) should be considered.

The use of an ultra-filtrate made from liver-pancreas-placenta-small intestine-mucosa (LPPM) seems to be most beneficial. This preparation is presently not yet available for general use due to the complicating manufacturing requirements and because it has not yet been registered.

Nutrition, enzyme substitution and *cell regeneration* by injection implantations together form the basis for a therapy strategy, which opens new horizons in the treatment of degenerative diseases for which no therapy has been available until now. Although we do not as yet have air-tight evidence at our disposal, the experiences gathered so far nevertheless prove that this concept is far more than just a hope.

The management of the treatment can be summarisized as follows:

1. Injection-Implantations

In order to initiate a amelioration or restauration of the instinal resorption and the cellular utilization functions injection-implantations with fetal or juvenile lyophilisated cells are applied. The following organ-preparations should be injected subcutaneously: →

At the moment it cannot be determined if and what time-intervals further implantations will be required. The recommended interval is 5–6 month.

Fetal small intestine (Mucosa) 100 mg
Pancreas 100 mg
Liver (fet) 150 mg
Hypothalamus 100 mg
Adrenal gland (acc. to sex) 100 mg
Placenta (acc. to sex) 150 mg

2. Regulation of the digestive functions

As substitutions for decreased activities are to be taken enzymes of plant- and animal-origin orally. →

A decisive factor in the restoration of the intestinal-mucosa-function is a cell-free lyophilisate consisting of liver, placenta pancreas and small-intestine mucosa. This preparation is to be taken before the breakfast on the tongue, primarly daily, later on intervals of 2 to 3 days. →

Wobenzym®
4–8 tablets daily as a source of vegetable enzymes
Bilibombin®
1–3 tablets daily as a fatsplitting enzyme
Vitafestal®
1–3 tablets daily as a combination of digestive enzymes, vitamins and trace-elements
LPPM - cell-free ultrafiltrate of fetal Liver, Pancreas, Placenta and Mucosa.

3. Diet

The treatment has to be supported by corresponding nutritional measures. The following rules are recommended:

The nutrition should be low in ✸animal proteins. If animal proteins are used, they should be taken in small quantities and come from fresh sources. Undenaturated milk and egg dishes are especially suitable protein sources. Three times weekly or daily a raw beaten egg or an egg mixed with juice should be taken. Further not preserved (canned) calv, beef, chicken and fish is recommended.

The ✸ *fat*-composition of the food should contain more plant-fats than fats of animal-origin. The best sources for the hightly-unsaturated fatic-acids are: sunflower-oil, soja-oil. The only known sources of the precusor gamma-linolic acid are breast-milk and prime-rose-oil. To avoid are pork-fat and all preserved and denaturated fats.

To ✸stimulate the digestive processes fresh, naturally maturated fruits or fruit juices should be taken before the meals. To favour are enzyme-enriched fruits like papayas, mangos, melons, pineapples, grapefruits a. o. If possible, a raw-food-diet (raw salades and vegetables) should be used once or twice a week.

It is very important to avoid all ✸ preserved, canned and denaturated foods including their additives and colors. These agents can probably play a role as releasing noxa.

Morbus Parkinson

Besides the therapeutic principles «stereotactic operations» and «Dopamin-L-Dopa», cell therapy comprises a treatment insufficiently used so far, although already F. ROEDER (1967) and A. C. GIANOLI (1969, 1982) mentioned the effect of lyophilisates of Substantia nigra.

An important condition of cell-therapy for Parkinson's disease is the principle of maintaining morphological structures. Of the 33 patients with evident bilateral Parkinson's syndrome treated by ROEDER, 25 responded with established statistical significance. The first achievement was an improved state of health, a stronger impulse, a retrogression of amimia and of the vegetative symptoms. The gait improved, rigor and tremor subsided. These effects reached their peak 2–3 weeks after the implantation of Substantia nigra and lasted about 2–3 months. The patients responding positively to the therapy got another two injections at intervals of 6 months. Generally, the effect of the second injection was still perceptible though not as distinct as after the first. Remarkably, no noticeable effect was obtained with the third injection. Of 33 cases treated, 8 showed no improvement.

These results are virtually confirmed by GIANOLI, who emphasizes the possibility of combining cell therapy with the dopamin treatment.

From the corresponding infantile dyskinetic diseases it may be concluded that cell therapy using Substantia nigra is not wide enough. Additionally advisable is a combination of basal ganglia (50 mg), cerebellum (100 mg), frontal brain (100 mg) and placenta (150 mg); Adrenal tissue also wins on interest in Parkinsons disease. The partial reconstruction of basal ganglia function meantime could be confirmed in animal trials. This biological therapy can well be combined with the pharmacological

treatment (L-DOPA, Nacom® or Akineton) but should be used before a stereotactical operation because after the interruption of structures the effect necessarily remains restricted.

Depressions

According to J. BABILLOTTE (1978), a depression is characterized by disturbances in four fields:

change of the psyche;
disturbances of the vegetative system;
changes of the hormone balance;
so-called somatic sensations in the organs.

The changes of the psyche are defined by a depressed, anxious mood, accompanied by listlessness, insomnia, joylessness, uninterestedness, lack of resoluteness, feeling of absurdity, discouragement; associated with these symptoms are anxiety, internal tensions and worries about the future.

The vegetative symptoms are much differentiated, with insomnia at the beginning and in the centre. Vegetative false regulations affect also the cardiocirculatory system and the digestive tract.

No doubt, cell therapy for depression is more biological and causal than drugs, let alone electric shock. The tissue of choice is hypothalamus, but the spectrum ought to be completed by tissues from germ glands, placenta and liver, according to the symptoms.

As regards the hormones, depressive women suffer from a loss of libido with anorgasmy, uninterestedness in sexual life, often amenorrhoea, dysmenorrhoea. The endocrinic effects in men make themselves felt by loss of libido, disturbed potency, which may increase to complete impotence.

The somatic sensations often so difficult to interpret clinically, which BARTH found in 247 patients of 298, are registered in nearly every region of the body. Complaints in the zone of the head are reported for about half of the cases, for 40% in the extremities and for $\frac{1}{3}$ of the cases in the chest and abdomen.

Migraine

The many causes and pathological reactions of migraine make the subject of a comprehensive study by F. SULMAN (1979). After exhausting the medicamentous measures, SULMAN recommends cell therapy where other methods have failed. According to him, cell therapy is still promising in such cases. J. BABILLOTTE extends the indication of cell therapy for migraine by placing cell therapy over medicamentous measures in cases of migraine. The tissues of choice are: placenta, thalamus, frontal-temporal-lobe, adrenals, gonadal tissue.

The apallic syndrome

Apallic syndrome (term created by KRETSCHMER) means central nervous lesions with loss of the pallic functions (pallium = cerebral cortex). Whilst the vital reflex mechanisms in the brain stem (circulation, breathing) still work, no sensory or sensitive stimuli enter consciousness so that no reactions controlled by consciousness can take place; the function of the «cerebral cortex» has

been lost, the functions of the brain stem are, partly, maintained. The full aspect corresponds to a «decerebration» with the clinical consequences of the decerebration rigidity. If certain reactions of the cerebral cortex – though abortive – are still traceable, the term «Coma vigile» is more adequate.

In the clinical aspect, the apallic syndrome is characterized by general listlessness and immobility due first to muscular atony, later muscular hypertonia. In serious cases, there are no corneal reflex and light reflex of the pupils, no deglutition-reflex and no buccal reflex. The functions of the central nervous system are reduced below the reactivities existing at birth. The eyes are open, vacuous, staring, mostly directed to one side above (fig. 260, 262). Optical and acoustic stimuli are neither registered nor answered, tactile stimuli may be perceived but cannot be answered either.

The course

is characterized by the rigor of decerebration. Part of those affected by acute insulti die within hours or days. In question are usually lesions reaching beyond the pallium i. e. involves the brain stem. The artificial control of breathing, cardiocirculatory function, heat-balance and nutrition, has in the majority of cases temporal limits, which cannot be mastered by methodical techniques.

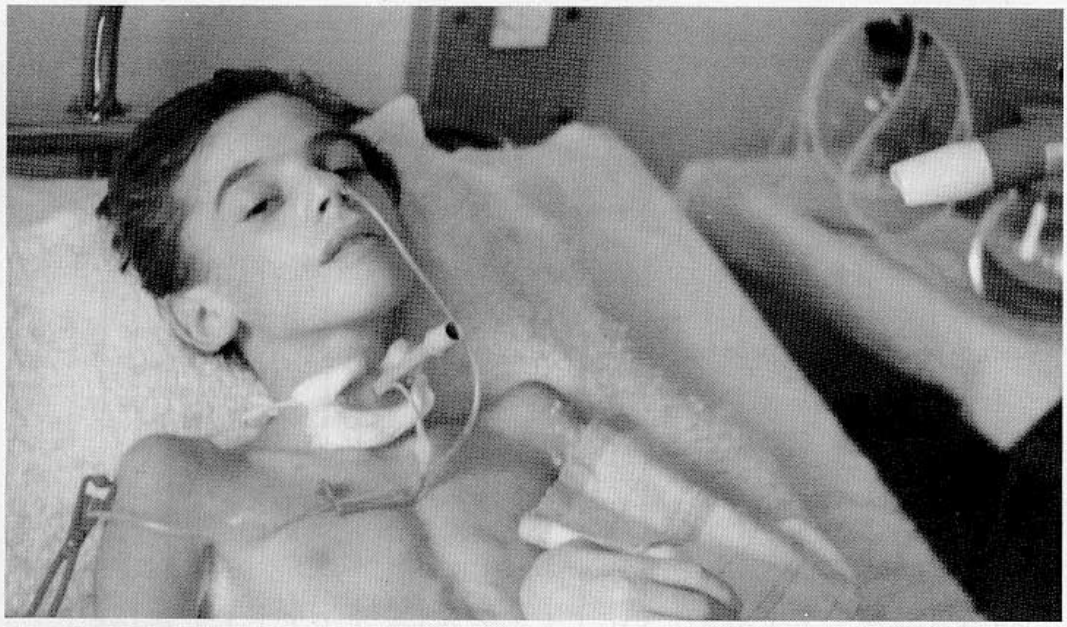
If the vegetative functions continue and the pallium functions subside, the chronic condition corresponding to the full aspect of the apallic syndrome develops: no reaction to optical, acoustic and tactile stimuli, tetraparesis or tetraspasm (fig. 272), growing marasm, trophic disorders (incl. cutaneous ulcers), lowered resistance to infections. The condition may be complicated by focal or generalized spasms, vomiting attacks, constipation difficult to influence.

The shorter the apallic condition the greater the chance of a rapid and complete return of the central-nervous functions. But only few are likely to have such a favourable course i. e. the short apallic conditions are seldom referred to as «apallic syndrome». The latter term ought to be reserved to apallic lasting conditions, namely the cases that stay apallic for weeks and months remain stationary or grow worse. Unconscious motor-automatisms (bending and extensor synergies, motions of the look and head, wiping and lacing-up movements, F. BROSER) and primitive answers to stimuli may occur, without any fundamental change of the condition of decerebration. The apallic syndrome fixed for weeks and months passes for a therapeutically uninfluenceable final stage.

As to the genesis

of the apallic syndrome, 2 mechanisms have to be distinguished as a matter of principle:

1. *Acute lesions of the central nervous system* cause serious destructions of the cerebral architecture and extinguish the functions of the cerebral cloak (decerebration); in the case of survival, a neurological final stage likely to be individualized by secondary symptoms is reached.
   This form is caused mainly by traffic accidents, incidents due to anaesthesia, acute encephalitis, strangulation, anoxia (especially in stenosing laryngotracheobronchitis). Remarkable is the fact that among 22 observations anamnestically in 5 cases the onset of the apallic condition coincides with a cerebral angiography. The possibility of an additional cerebral lesion by extravasating high-percentual opaque matter from the (injured, ruptured) vessels should be included more ex-



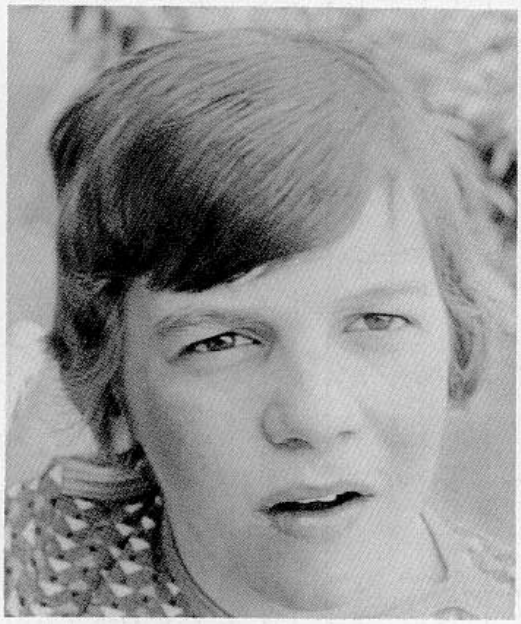


Fig. 272:
Courses of an apallic syndrome: physiognomy.

a) R. M. after a five-month apallic condition with nasal tube for nutrition, trachea-canula and bladder-catheter.
b) Condition of the boy 8 months after the therapy described in the test.

Haben einige Kinder, oder auch Erwachsene das apallische
Syndrom, wie ich? Wenn nicht, dann ist es auch nicht schön.
Ein ¾ Jahr war ich dort im Stadtischen Krankenhaus, von Arzten
operiert, gepflegt. Und ich danke ihnen dafür, daß sie
mich gesund gemacht haben.

Fig. 273:
Specimen of hand-writing by a 12-year-old boy, who was in a complete apallic condition for 5 months; finished the teaching matter of the 5th elementary school after 3 years of treatment.

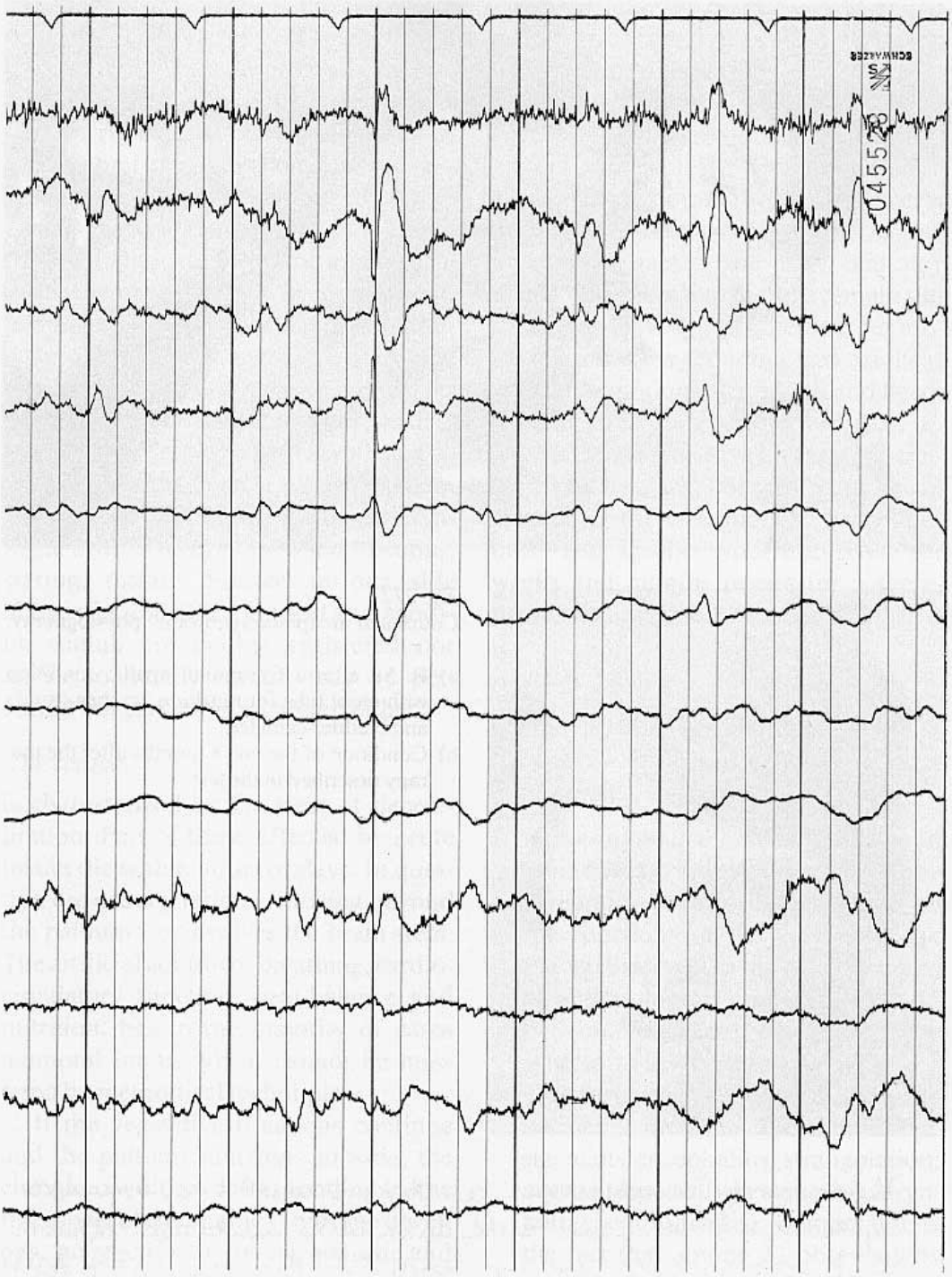
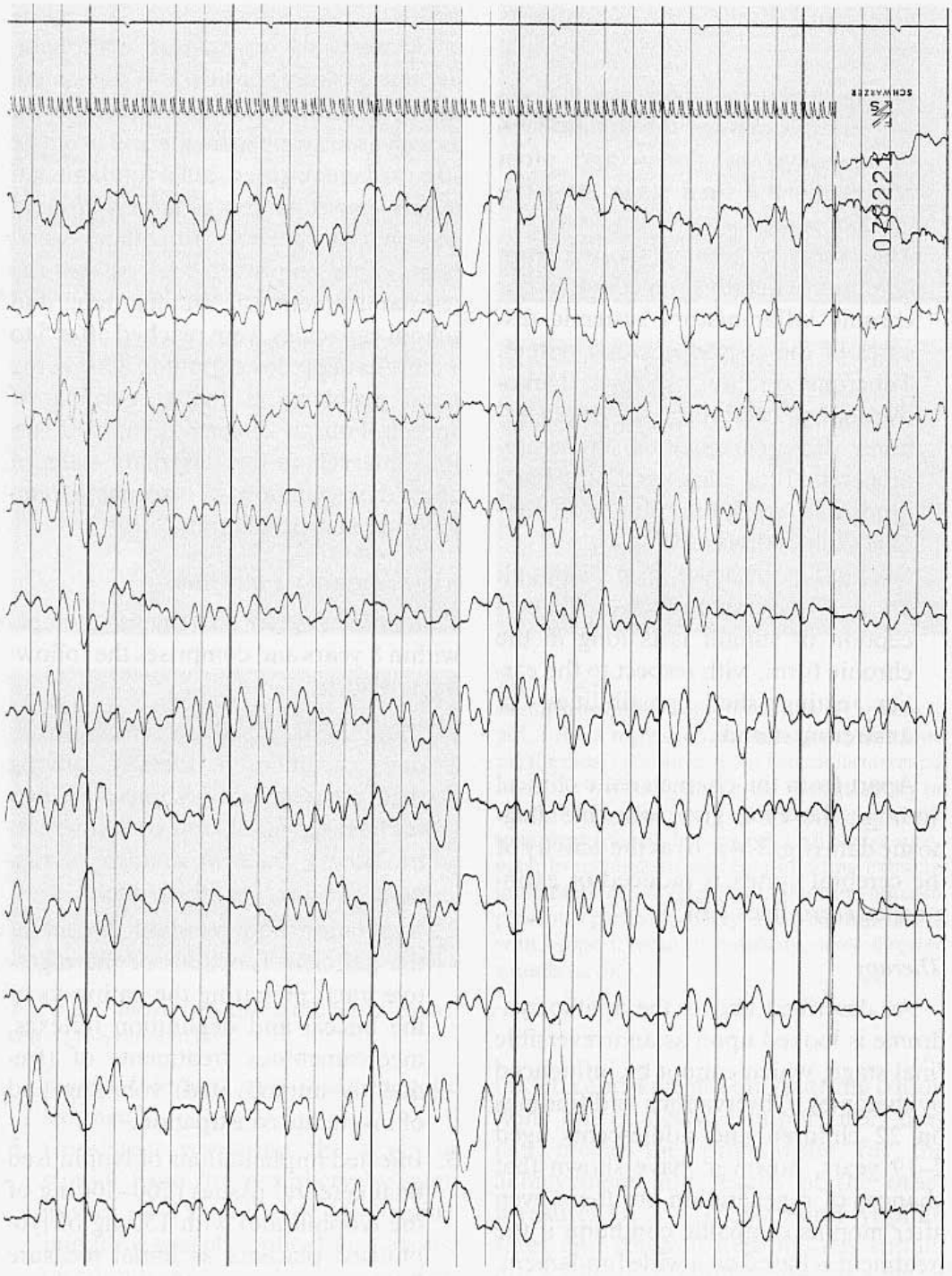


Fig. 274 a, b:
Differences of EEG in amplitude and ground rhythm after 11-month apallic condition (a) and after 17 months of treatment (b); case as per fig. 283.


SCHWARZER
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actly into the indication of angiography.

2. *Owing to chronic diseases of the central nervous system*, the apallic syndrome develops slowly and often constitutes the final stage after the lapse of years.
   This form originates mostly from heredodegenerative metabolic or chronic inflammatory systemic diseases of the central nervous system. Tuberous cerebral sclerosis, leukodystrophy, cerebroretinal degenerations, leukoencephalitis, hyperammonemia, final stages of Louis-Bar's syndrome constitute the most frequent initial diseases.
   Whereas in the acute form no stimuli are perceived or answered, the perception of stimuli lasts long in the chronic form, with respect to the earlier extinguished possibilities of answering stimuli.

Apart from the characteristic clinical findings, the EEG gives valuable diagnostic data (fig. 274 a, b) as the activity of the cerebral cortex is reduced or extinguished (zero-lines EEG).

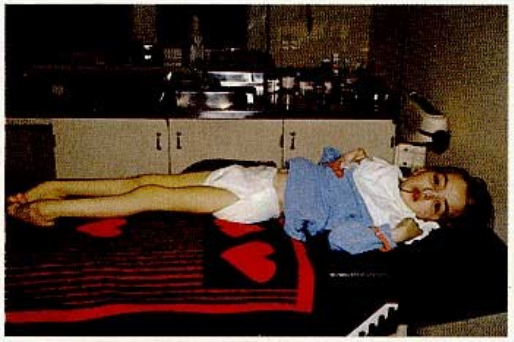
Therapy

As described above, the apallic syndrome is looked upon as an irreversible final stage, which cannot be influenced by therapies. Observations and findings on 22 children and adolescents aged 2–19 years, however, have shown that chances of regeneration are there even after months of apallic condition if the treatment is based on a wide fundament. This applies only to the acute apallic conditions, not to the heredogenerative final stages: The therapeutic outcome varies and seems to depend on the patient's age. Unfavourable is the age up to the ripening of the medullary sheath i. e. the second and third years. In 2 children of this age (1 × strangulation; 1 × anoxia by stenosing laryngotracheobronchitis) spasms were considerably alleviated, the deglutition reflex and buccal reflex as well as answers to tactile and acoustic stimuli were restored, but a fundamental improvement of the general condition was not achievied. In other cases, remarkable improvements up to the re-establishment of the learning and school capacities were reached after 5 to 9 months of apallic condition. One of the main problems is the re-learning of speech. Four of 21 cases died, after various intervals in the stationary state, of acute dysregulations of respiration, temperature and circulation.

The therapeutic conception

took shape after reluctant attempts within 8 years and comprises the following measures:

1. Elimination of all dispensable residues of intensive therapy, among them the removal of esophageal tubes for feeding (nasal, oral, operative gastric tubes), tracheal canules, permanent catheters for the bladder.
2. Regulation and re-establishment of the deficient functions of the digestive tract: preparing the pathways of the buccal and deglutition reflexes, medicamentous treatments of (frequently unmotivated) vomiting and of inveterate constipation.
3. Injected implantations of lyophilised fetal cerebral tissues (200–300 mg of the lyophilisate) with 150 mg of lyophilised placenta as initial measure for the regeneration of the central nervous system.
4. Injections of cerebral hydrolysates (cerebrolysin 1–3 ml daily for 3–4 weeks) combined with amino-acid and lipid infusions at intervals of 2 days. Lipid infusions are sometimes



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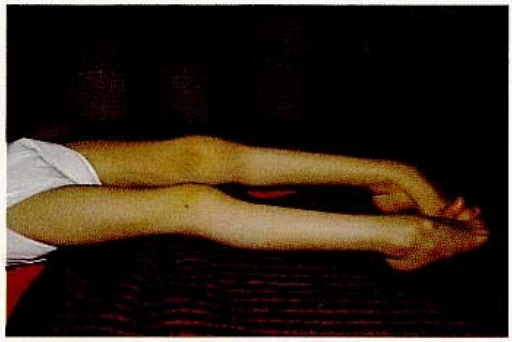

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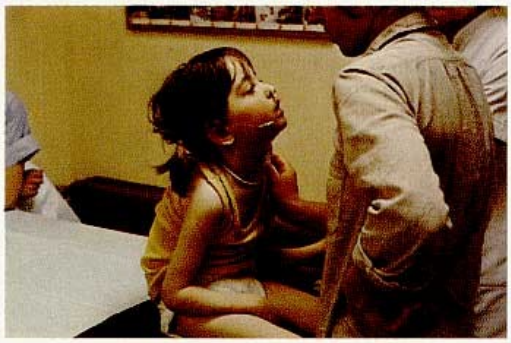

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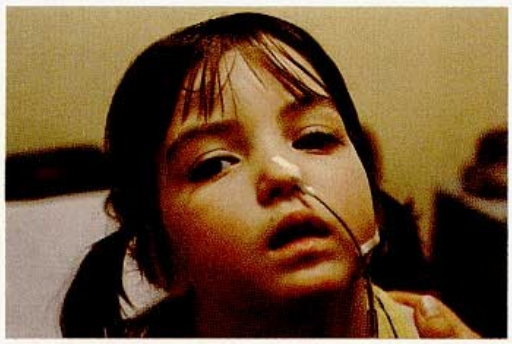


d

Fig. 275 a–d:
Metachromatic leukodystrophy in a 5-year-old girl. After a regression period of two years loosing the most centralnerveous functions no reaction to the environment, severe tetraspasticity (a, b). 6 month after starting a multidimensional treatment (physiotherapy; diet; digestive enzymes; liver-pancreas-placenta-intestine extracts; implantations of fetal liver, intestine-mucosa, placenta) partial recovery: head control, sitting with support, reduced spasticity, some directed sounds (c, d).

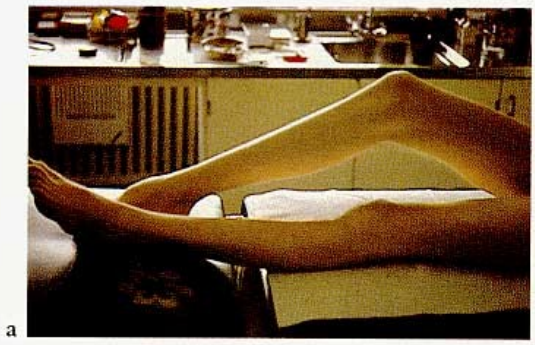
Fig. 276: Tuberous sclerosis with adenoma sebaceum; 13-years-old boy.

poorly tolerated and must then be stopped.

5. Consistent preparing the way for stimuli from the periphery by gymnastics (2–4 × daily for 15–20 min), initiating speech, optical and acoustic stimuli (music, television, conversation).
6. Posture measures adequate to the stage of regeneration and supply of auxiliary apparatuses.

For the break-through of the apallic state, the biological measures mentioned under 3 and 4 are not only starting conditions but of decisive importance; they can create the prerequisite for the achievement and results of the other measures (1, 2, 5, 6). Cerebral lyophilisates and cerebral hydrolysates should not be used if apallic states as part of heredodegenerative diseases of the central nervous system are in question.

The therapeutic outcome
depends on the consequency of the measures described, on the kind and extent of the lesions and on the age. The



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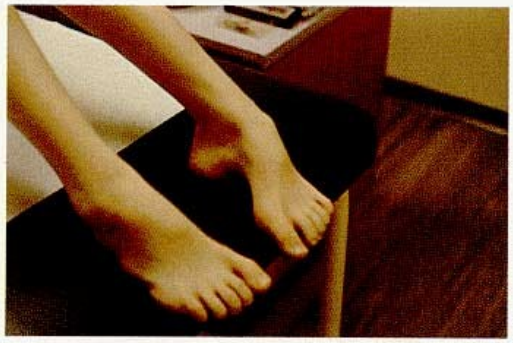

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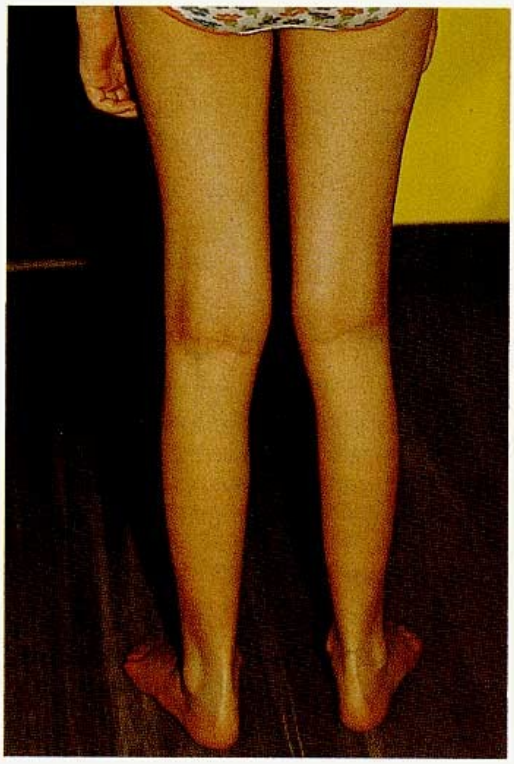

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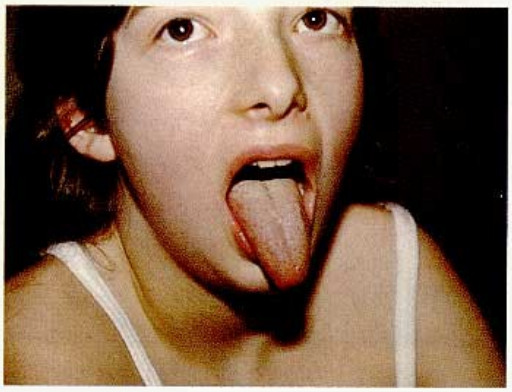

Fig. 277:
Caved foot and periphereal muscle atrophy in a 15-years-old girl with *Friedreichs Ataxia*.

Fig. 279:
Carnithin-deficiency-disease with muscle atrophy, reduced walking and lost stair-going capacity in the age of 14 years (a); During 2 years of a multidimensional treatment a satisfactory recovery of the muscle functions (b).

Fig. 278:
«Snow tongue» as a symptome of intestinal disorders in many degenerative diseases of nervous system and muscles. 14-years-old girl with progressive muscle dystrophy, scapulo-facial type.

duration of the apallic syndrome seems to be of minor importance as in certain cases (fig. 272, 275, 277) apallic «final stages» of 3–11 months can still bring about astonishing restitutions. Exactly, every individual case ought to be represented separately; but the observations made in the stage of regeneration provide very valuable conclusions on the topographical points of apallic lesions.

In contrast to the opinion that chiefly nerve cells perish and the condition is irreversible, the long-term observations specially of the traumatic forms suggest that mainly the secondary structures of the neuropils (dentrites, neurites, medullary sheaths, synapses) are affected. The following arguments may substantiate this:

a) The re-establishment of the functions follows much the sequence of the acquirements of these functions in infancy and babyhood; the speech provides more difficulties than the rough statomovements whereas words are well understood.
b) The memory, which must be supposed to be seated in the cytoplasm of the neuron, persists largely and in many details even if interrupted for several months by the apallic state.
c) Even abstract areas remain (a boy e.g. learns to speak only indistinctly after 5 months of apallic condition with zero lines EEG after acute dysmyelinisating encephalitis, but reckons quickly and with reliable correctness using dominoes).
d) The memory returns up to the time of the loss of consciousness and sets in three weeks after the beginning of the treatment (examples fig. 272, 275, 277).

The therapeutic results are influenced by the final failure of important perceptive organs e.g. by atrophy of the optic nerve. Focal onsets, which may call for anticonvulsive treatment, occur frequently in the stage of regeneration. Ground activity and re-ripening of the graphic elements in the EEG do not correspond to the clinical findings.