Looking at the elementary structure of the central nervous system, the neuron, we can see basically three processes:

a) a deficit in neurons;
b) an impairment of maturation and differentiation of the neuropile;
c) destructive (degenerative) processes.

Mental impairment constitutes by far the most important proportion; it goes back to an impairment of maturation of the central nervous system on account of which the functional state of the brain remains in the stages of early childhood. Several points of approach are offered for therapy applicable to this condition, which is known clinically under names such as «brain damage from early childhood», «infantile cerebral palsy» or «cerebral motor disturbance» (fig. 261).

1. *Nonspecific Stimulation of the Metabolism* through increased supply of substrate; in most instances a better supply of blood to the brain is achieved. These agents have so far been used predominantly for elderly people and not sufficiently utilized for children. They include:

euphylin,
heart glycosides,
caffeine,
amphetamines,
complamin,
ephedrine derivatives,
camphor and others.

2. *Specific influences on metabolism* by agents which selectively stimulate individual metabolic processes in the neuron. This field has been neglected by pharmacology and clinics for a long time; it is still in its infancy since sufficient clinical experience can support the theoretical basic concept only in the case of a few substances. The biocatalysts include

a) Pyritinoldihydrochloride monohydrate (Encephatol);
b) Piracetam (Normabrain, Nootrop);
c) Centrophenoxin (Helfergin);
d) Actihaemyl;
e) Nicotinic acid derivates;
f) Membrane activators;
g) Monoamino-oxydase inhibitors;
h) Adrenocorticotropes hormone (ACTH);
i) L-Dopa.

3. *Biological Organ Therapy («Brick-Therapy»)*

Up to the present biological substances of various biochemical dimensions have not been available to a sufficiently great extent for the stimulation of the metabolism of the neurons, for repairing and synthesizing defective and unmatured neuron structures; more-

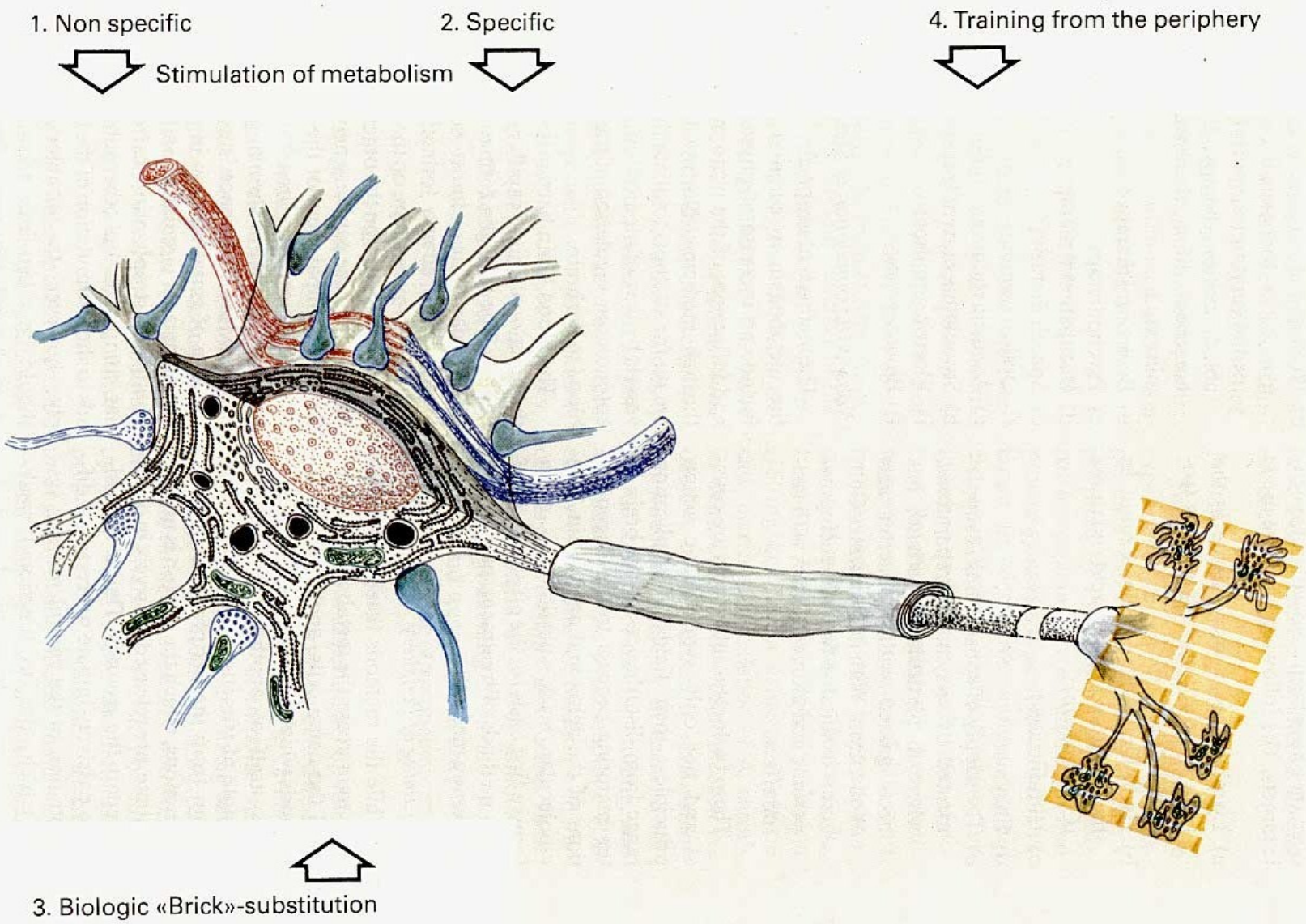

Fig. 261: Therapeutic approaches on the neuron

over, they have been used without specific targets. The following types are used:

a) Lyophilisates of brain tissue in the form of injection-implantations (so-called cell therapy);
b) Hydrolysates from animal brain in the form of amino acid mixtures (Cerebrolysin);
c) Ultrafiltrates;
d) Enzymes;
e) The supply of constituents is supplemented by enzymatic preparations, where in particular experience has been gained with Coliacron and Wobenzym. With its 3 enzymes Coliacron is suitable for influencing hypotonic and atonic muscles with lasting effect.

These biological substances are causal and not only symptomatic action principles; their fields of application range from disturbances of the brain in the maturing process to the degenerations of the aging and aged brain. The «molecular brick substitution» often forms a first basis for the effectiveness of other methods of treatment, particularly of training methods.

4. Training of Periphery

While the methods listed under 1–3 serve to increase the metabolism and rebuild the nerve cells, another group of methods which is differentiated in itself, avails itself of another principle: the principle of (functional) training of the neuron from the periphery. Sequences of functions, which the neuron is unable to initiate, are released passively in order to prepare the grounds. Thus it is possible to passively initiate processes of differentiation of the central nervous system which, due to functional weaknesses, cannot be realized actively. These methods include:

a) Physiotherapy (remedial gymnastics, gymnastics for special diseases, remedial eurythmics, sports for the disabled, motion therapy, therapeutic horseback riding, therapeutic swimming etc.);
b) Behavioral therapy;
c) Psychotherapy;
d) Occupational therapy;
e) Speech therapy;
f) Optical training;
g) Acoustic training;
h) Stimulating current therapy;
i) Electric impulses;
j) Bioenergetics.

Nonspecific stimulation of Metabolism

The methods of unspecific increase of the metabolism in cerebral affections include an increase of physical activity and influences of the brain metabolism through medicine. Narrow limitations are set for attempts to dilate the cerebral vessels by way of medication, due to the autonomous regulation of the supply of blood to the brain.

The blood-brain barrier is formed by the functional unit of capillary-astroglia-neuron. The astroglia formations envelop the capillaries almost completely. Swelling and edema formation in the central nervous system, on the one hand, and cicatrisations, on the other, lead to a narrowing of the capillary networks and thus to an impairment of the metabolic chain in the capillary area; this is due to increased volume or shrinking of the astroglia. More experience is available in the area of geriatrics than in pediatrics, with agents for circulation and the heart. The use of strophantine, caffeine, fludilat, complamin and other substances leads to short stimulation of the blood supply; however, the counteradjustment should be taken into account, which takes place after the main effect has subsided. For these considerations alone,

the methods of unspecific increases of the metabolism serve to treat acute conditions rather than chronic diseases of the central nervous system.

A very important way of nonspecific influences on the brain-metabolism is a disease-orientated-nutrition and diet.

Specific influenser on the metabolism of the Central Nervous System

The intent to increase the performance of the brain goes back to time immemorial; it ranges from the pneuma of GALEN of BERGAMON over the mixture of ether and spirits of Friedrich HOFFMANN (1760, Halle) (in the form of ether drops, used up to the present century) to the «modern» *psychostimulants, psychoenergetica* and *nootropica* (J. KUGLER, 1977). The first specific entry was made by LEVIN (1927) with *amphetamines*, which increase the ability of perception, concentration and reaction. Similar, though shorter improvements of performance of the central nervous system can be achieved with *coramin, ephedrin* and the previously much used *camphor.*

The practical applicability of these substances is limited because, in part, they cause dependence and addiction; without exception, they lead to a counteradjustment, a reduced performance of the central nervous system, after a stimulated stage which may last minutes or hours.

A few substances affecting the brain metabolism do not result in such a counteradjustment; their focus is more specific than the above mentioned substances and the agents that have the general effect of encouraging circulation (cardiac tonics and circulatory stimulants).

In theory and clinical practice certain substance groups, to which specific metabolic stimulation must be ascribed in experiments on animals and humans, have found general acceptance during the last two decades.

Pyrithioxin, Pyritinol (Encephabol®)

The probably most comprehensive experimental materials and clinical experience with a neurodynamic agent are provided by Pyrithioxin (Encephabol). An increase in glucose utilization and protein synthesis is attributed to this vitamin B6 derivative without vitamin character. Probably this does not do full justice to its complex mechanism of action. Before evaluating the therapeutic importance the experimental data must be analysed. In previous basic pharmacological examinations (HOTOVY, R., ENENKEL, J. H. a. o., 1964), Pyrithixion (150 mg/kg) had a calming effect on cats, increased circulation of A. carotis in dogs, connected with a nitrogen reduction in the urine, a diminishing experimental catalepsy in cats, an improved training of rats for running, and an increase in the psychomotoric efficiency in persons. Circulation and visceral organs remained unaffected. There were no criteria of central stimulation such as an awakening effect, locomotoric action and tremor which are particularly characteristic of amphetamines.

Membrane Effects

In hemolysis experiments on human erythrocytes, MARTIN succeeded in starting, in vitro, a monophasic reversible labilisation of the erythrocyte membrane; the membrane-stabilizing action of benzyl alcohol was antagonized by Pyrithioxin derivatives. The antialcohol effects oberserved in vivo may be bound up with these membrane-influencing properties. The choline transport through the membranes of human erythrocytes and in synaptosome preparations from rat brains is inhibited. The retardation of the c-AMP-synthesis with

procaine – checked on brain sections of rats – is antagonized. The last two findings show that the membrane effects of Encephabol are not confined to erythrocyte membranes but can also be demonstrated on neuron membranes. The protective mechanism against alcohol is also assumed with regard to the cholinergic spinal marrow synapsis (BENECKE a. o. 1972).

ENDO assumes that Pyritinol influences the interplay of phospholipid-protein substances; the extractability of firmly bound phophorus lipids increases. Membrane permeability increases; some substrates such as for example sodium, glucose, choline, are transported easier.

Clinical Effects

The short-time memory and the immediate memorization in 48 persons subject to experiment was markedly improved according to investigations by I. M. DEUSINGER and H. HAASE (1972) under 300 mg of Pyrithioxin daily for 4 weeks. Increases in vigilance in school children, 8–13, were substantiated by K. D. STOLL (1973) by way of concentration tests after administration of Pyrithioxin. G. LOGUE and others (1974) reported on further positive action on learning attitudes; Ch. FEHLING-JOSS reported on such effects with dyslexia (1974).

Additional effects were registered with regard to brain contusions (BYSTRICKY a. o. 1977; S. Y. OH 1974; LAHODA), with the appalic syndrome (K. v. WILD and G. DOLCE, 1976), with organic psychosyndromes (MISUREC and others, HAMOUZ, W., 1977), with chronic alcoholism (J. MASARIK and J. DEMEL 1974). The probably most interesting interactions were found with cerebral seizures. The consequences on cerebral seizures were examined by GASTAUT on 48 patients with a double-blind experiment. In 5 cases a reduction of the seizures was noticed, in 5 cases an increase. The electroencephalogram changed in the Encephabol group in 8 cases, among them 5 cases changing toward the positive; in the placebo group the change was noticed in 2 cases. On the whole, interest, language, academic and occupational performance were judged favourably. TASSINARI did not see any influence on the electrocardiogram in 30 seizure conditions, when Encephabol was administered intravenously. A differentiated study of infantile seizure conditions (43 cases of 4–14 years) was made by ROGER, ROBAGLIA and C. DRAVET. In a pyridoxin insufficiency test conducted by means of tryptophane loads, 22 of these children were subjected to pyridoxin insufficiency; a negative test was made with 21 of the children. Administered were 300 mg (600) daily for several weeks. In a group of 21 children who were not free from seizures during the experiment, the seizures were reduced in 7 instances, and increased in 13 instances.

According to DIEMATH pyrithioxin effects can be noticed after 4–6 minutes in the electroencephalogram, but they remain confined to the depth branches and are reversible in a few minutes.

Precisely these seemingly contradictory results in seizure conditions and the effects on the electroencephalogram suggest that pyrithioxin is a substance which acts on the neuron specifically and in a highly efficient manner. The mechanism of action is most probably of complex nature; the increase in membrane permeability is probably only at the beginning of the metabolic chain; only on account of this it is possible to improve the cytoplasm metabolism. Since the initial substance, Vitamin B_6 attacks at 6 different points the trypto-

phane-serotonine metabolism, the B_6 derivative pyrithioxin could play a similar role. The positive action in hypodynamic disturbances (Down's syndrome, hypotonic cerebral paralysis, impulse insufficiency), on the one hand, and an increased effect in hyperdynamic conditions, on the other, suggest a pharmacodynamic emphasis in this metabolic chain.

Piracetam (Nootrop®, Normabrain®)

This is a derivative of the *gamma aminobutyric acid* to which an improvement of the synapsic function is attributed. In animal experiments it was possible to shorten the hypoxic recovery times, to prevent hypoxy-contingent cancellations of short-time memory, and to improve learning effects. In the clinical field various authors observed impulse increases and depression-reducing effects (KANOWSKI1975). My own observations among more than 1000 children suffering from cerebral retardation extended over 10 years; they were made in a nonsystematic examination series and gave some enlightenment on the effects and limitations of application. The incorporation of piracetam in the therapy for hypodynamic cerebral paralyses and mongolism is probably advantageous between the second half-year of life and the end of the second year. Symptoms such as slowness, poor initiative, weak power of concentration can also be influenced in a positive way among older children. On the other hand, hyperactive erethitic children can respond already under lower dosages (1/4 measuring spoon, 100–200 mg daily) with increased restlessness and excitement; even with a onetime administration in the morning it may be possible that sleeplessness will occur. With the single individual these oberservations can be reproduced by several starts of administration and discontinuation, so they have practical significance.

The indicative range of this surely interesting substance deserves to be given a better analysis.

Centrophenoxin (Helfergin®)

This is a synthesis product from an aminoalcohol and p-chlorphenoxy-acetic acid. In animal experiments the influence on cell respiration and glucose metabolism has been established (K. NANDY). Without changing pulse frequency and blood pressure, an increase in spontaneous activity has been achieved in animals. The lipofuscin formation, a morphological expression of the aging process in the cytoplasm of the neurons, seems to be delayed by centrophenoxin. The ability to learn and to remember were increased and the life of C47BL/6-mice was prolonged (K. NANDY, 1977). Lipofuscin is considered a degeneration product of the mitochondriae (P. GLEES 1977), the intracellular digestion of which is more difficult for older cells than young ones. S. RIGA and D. RIGA (1977) attribute even a lipofuscinolytic action to centrophenoxin. RODEMANN and BAYREUTHER(1977) registered, under specific experimental conditions, a significant increase in the metabolism of glial-cells in humans. Contingent upon dosage and duration, centrophenoxin activates the pentosephosphat-cycle (making ribose-5-phosphate available for the nucleotide and nucleic acid synthesis) and influences the transport of specific nucleic acids from the cell nucleus into the cytoplasm (K. KANIG, 1977). S. HOYER and K. KENDEL as well as R. COIRAULT have pointed out the increases in cerebral insufficiency circulation.

In the clinical field influences of centrophenoxin were ascertained on the aging process (J. BÖGER, 1977), by way

of flicker-photometric examinations; it had also influence on children with learning difficulties and legasthenia (PERET, WEHRLI and HAFEN, 1977). According to HOYER, a significant increase is achieved by centrophenoxin among children suffering from a pathologically reduced brain circulation. This lets us visualize effects with the organic psychotic syndrome to be within reach. In the treatment of mongolism HAUBOLD included Helfergin in the basic therapy, probably with the idea of delaying a premature aging process and increasing the neuron metabolism.

Actihaemyl

This is a haemodialysate from the blood of young calves; is contains approximately 30% organic compounds and about 40–45 mg/ml dry substance. The organic share contains amino-acids, nucleic acid components, low-molecular peptides and substances of the intermediary metabolism – glucose, acetate, lactate, hormones.

An improvement of transport mechanisms of oxygen and glucose, a stimulation of the cell metabolism and of the cell regeneration are attributed to actihaemyl. In particular, it is said to have the following effects on the cellular metabolism, inclusive of the neurons:

Increase in activity of key enzymes of the respiratory chain.
Increase of the intracellular stock of energy-rich phosphates;
Diminution of pathologically increased lactate and pyruvate values;
Increase of the oxygen transport to the cell;
Increase of the glucose transport.

Actihaemyl is a biological medicine free from side-effects; it may be administered at a dosage of 100–300 mg daily the oral way. Under seriously traumatic and apallic conditions of the brain, the dosage administered may be up to 1000 mg a day parenterally.

Nicotinic-acid derivatives

Nicotinic acid compounds lead to a relatively speedy improvement of the blood circulation at the peripheries. Whereas the improvement in circulation in the central nervous system is problematic, distinctive pharmacological effects on the central nervous system have been secured with regard to nicotinic acid amides.

Niamid® = 1-/2-benzylcarbamylethyl 1/2-isonicotinoylhydrazin is an effective monoamino-oxydase inhibitor with remarkable metabolic and psychotherapeutic effects. As part of the basic therapy of mongoloid children and in other hypodynamic symptoms of mentally retarded children it is possible to improve the psychomotoric activity, social contact and emotional control.

Similar effects can be expected from the following preparations: Hämovanad® (= Inositolnicotinate) and Nicoacid® (= sodium nicotinate), Progresin fortard® (= Mg-nicotinate), Nicoplectal (= 50 mg of nicotinic acid + 200 mg of buckeye extract).

L-Dopa

A favourable effect on certain cases of dyskinetic cerebral paresis, besides an influence on Parkinson's disease, is ascribed to L-Dopa (Nacon®) (SIEVERS, 1980)

Membrane Activators

These are substances and biocatalytic combinations intended to improve the functioning of the cytomembranes. Membrane disturbances play their part in numerous congenital disorders of the metabolism and in the aging process of the tissue. Following are the areas of indication:

a) Physiological and premature aging processes;
b) innate metabolic disturbances caused by the membranes;
c) Down's syndrome (basic treatment);
d) Hypothyreosis-athyreosis.

The function of the membrane activator is not confined to supplying intracellularly lacking or reduced substances; it also creates the premises for transmembral movement. Numerous preparations and combinations of vitamins, trace elements and biocatalysators increasing the blood circulation aim at this effect.

Long years of practical experience with various individual constituents have resulted in a biocatalytic combination which is available as *Membravit®*; it contains 3 magnesium compounds, zinc, iodized common salt of Tölz compound, vitamins B1, B2, B6 and tryptophane. The substitutes magnesium and zinc activate the DNS and membrane metabolism in connection with asparagin and orotic acid. The B-vitamins catalyze numerous enzymatic processes, for which magnesium and zinc are essential co-enzymes. After all, the metabolic chain of tryptophane to serotonin can only function if tryptophane is offered to a sufficiently great extent and is also transported into the cell.

Biological Therapy

Decisive progress in the treatment of mental development disturbances was achieved in the last 20 years by the introduction of the so-called cell- and enzyme therapy into the therapeutic concept. The offer of fetal cell suspensions serves to maturate secondary structures of the central nervous system – dendrites, neurites, medullary sheaths, synapses. Naturally, nonexisting cells cannot be replaced. This «Brick-component» therapy in the form of lyophylised fetal cerebral tissue, i. e. the offer of substrates, is supported by the stimulation of the incorporation, namely enzyme therapy. Whereas substrate preparations are available in sufficient differentiation, the availability of enzyme preparations is still fragmentary. The possibilities and limitations of both therapy methods which complement each other, will be briefly described hereafter.

Injection Implantations (Cell therapy)

The following process is initiated by deeply subcutaneous (epifascial) injection of cell and tissue suspensions of xenogenic fetal cerebral regions, in the organism of the recipient:

1. The fetal heterological donor material contains a high concentration of organ-specific substrates and enzymes which is characteristic of rapidly growing embryonal and fetal tissues.
2. The injected suspended tissue material is dissolved like a net within two hours in an animal experiment intraperitoneally, decomposed and attached to the microphage membranes as tissue particles; a leukocytosis develops in the peripheral blood picture.
3. The complex of microphages (= polynuclear) + tissue particles is subject to a phagocytosis during the following hours, through macrophages (monocytes, histiocytes); in a kind of « microphage battle» the complexes are intracellularly decomposed in the macrophages. The process is completed after 48 hours to such an extent that optically no

Symptom	CENTER OF LESION	*recommended cell suspensions for implantation*
Intelligence normal		
Debility (iQ 80-50)		*cortex, hemisphere, frontal-, temporal-,*
Imbecility (iQ 50-20)		*parietal-, occipital brain*
Idiocy (iQ ander 20)		*according to cause and conc. symptoms*
normocephalic		
macrocephalic		
microcephalic	CEREBRAL CORTEX	
Monoplegia	CEREBRAL	
Diplegia spast.	HEMISPHERE	*cortex, hemisphere, frontal-, temporal-,*
Hemiplegia limp.		*parietal-, occipital brain*
Triplegia		*possibly diencephalon spinal medulla*
Tetraplegia		*according to cause and symptoms*
Contractures		
Rigor		
Muscle-Hypertonia		
Muscle-Hypotonia		*mesencephalon, occipital brain, Medulla oblong.*
Dystonia (alternat. Tonus)		*mesencephalon, occipital brain, Diencephalon*
Convulsions		*Petit-mal: mesencephalon, Medulla oblong., Thalamus, cerebellum*
Hyperkinesia		*Grand-mal: cortex or sections*
Coordination-Discorders		*cerebellum, basal ganglis, Diencephalon, cortex*
Tremor		*basal ganglia, Diencephalon, cortex*
Chorea	BASAL GANGLIA	*diencephalon, basal ganglia, temporal brain*
Athetosis		*frontal brain, basal ganglia, temporal brain*
Restlessnes	DIENCEPHALON	*diencephalon, basal ganglia, temporal brain*
Eretism		*Thalamus, basal ganglia, temporal brain*
Autism	HYPOTHALAMUS	*Hypothalamus, diencephalon, frontal brain, hemisphere*
extrapyramidal Symptoms		*basal ganglia, diencephalon, mesencephalon*
Initiative-Disorder		*frontal brain, diencephalon*
Concentration-Weakness		*thalamus, diencephalon, cortical areas*
Emotional Incontinentia		*Hypothalamus, diencephalon, cortex*
Perseveration		*diencephalon, cortex*
Legasthenia		*hypothalamus, diencephalon, cortex*
Polydipsia		*diencephalon, hypothalamus, hypophysis*
Polyphagia		*diencephalon, hypothalamus, hypophysis*
Hypertrichosis		*diencephalon, hypothalamus, mesencephalon*
Vegetative Disorders		*mesencephalon, Medulla oblong., diencephalon*
Trophic disorders		*mesencephalon, Medulla oblong., diencephalon*
Lability of temperature		*mesencephalon, Medulla oblong., diencephalon*
Hypersensibity	MESENCEPHALON	*mesencephalon, Medulla oblong., parietal brain*
Hyposensibility		*mesencephalon, Medulla oblong., parietal brain*
Hyperhydrosis	MEDULLA OBLONG.	*mesencephalon, Medulla oblong., diencephalon*
Anhydrosis		*mesencephalon, Medulla oblong., diencephalon*
Ataxia	CEREBELLUM	*Cerebellum, diencephalon, frontal brain, basal ganglia*
Strabism		
Eye-Paresis	VISUAL DUCTS	*diencephalon, thalamus, occipital brain*
Nystagmus		
Reduced Visual-Capacity	OCCIPITAL BRAIN	
Amaurosis	EYE	*optic nerve, retina, lens*
Reduced Hearing-Capacity	HEARING DUCTS	*diencephalon, mesencephalon*
Deafness	TEMPORAL BRAIN	*temporal brain, occipital brain*
Dyslalia	EAR	
Swallow-Discorder		*basal ganglia, Medulla oblong., mesencephalon*

The most frequent symptoms of cerebral damages in early infancy have been classified roughly according to their o ligin in the central nervous system.

Fig. 262: Symptomatological implantation therapy.

foreign particles are any longer identifiable.

4. The intracellular digestion of the phagocytised complexes of microphages + donor tissue takes place in intracellular digestive cisterns (vacuoles). The main mass of the ingested tissues disappears rapidly from the digestive cisterns; remnants of the complex of microphage membrane + donor tissue particles are identifiable for a relatively long time (48 hours).
5. The bulk of donor material is rapidly moved away and utilized. Vital storage and radioactive taggings concordantly show the removal within the first 6 hours after implantation; the main contingent is moved away within the first hour.
6. Whereas the bulk of the donor material is handed over to the metabolic passages of the recipient (utilization), the smaller remaining complex of microphage membrane + donor tissue particles may have an immunogenic effect. This applies primarily to connective tissue structures (glia, mesenchyme).
7. Two premises are vital for the incorporation:
   a) There must be a need in the corresponding organ of the recipient (defect, illness, insufficiency).
   b) For the incorporation the biochemical components must have the corresponding organ-specific structure.
8. The incorporation can take place in accordance with the needs of the recipient by various dimensions; experimental evidence available ranges from oligopeptides to (heterological) macromolecules (immunoglobulin M).
9. The advantage of implantations by injection as against conventional transplantation techniques is as follows:
   a) the implanted tissues are not dependent on blood supply in the recipient; they do not suffer any structural changes on account of degeneration as a result of a lacking blood supply and anoxaemia.
   b) the implantation technique reaches organs inaccessible to conventional transplantations (e.g. brain, liver, pancreas, endocrine glands, thymus and others).
   c) the implantation technique alone can supply substantial quantities of biochemical substrates and enzymes of fetal tissues.
10. The clinical effect of the implantations by injection sets in during the third week after implantation in measurable way; it extends to 4 months up to two years, depending upon age, organ and basic illness.

In some organs (placenta, liver, suprarenal gland) a short immediate effect can be seen within minutes to hours after implantation.

Selection of implantation-tissue

In the case of disturbances of the central nervous system, the organ (= brain region) is selected by symtoms or symptomatological localisations. Fig. 262 provides a guiding survey for practical application.

The following principles used for implantation treatment have resulted from so far 70000 implantations on handicapped infants, children and youngsters:

A) The therapeutic expectations are the greater the earlier treatment is start-

Age	STATO-MOTORIC	FINE MOTORIC, COORDINATION	DRINKING, EATING, LANGUAGE, COMPREHENSION OF LANGUAGE
14			
13			
12			
11		uses knife for cutting	data learned «auditively» are utilized
10		copies geometric figures	repeats sentence of 20 syllables
		writes skilfully and fast	interprets material which was read or seen
9			spontaneous statem. w. compl. sentences
		catches flying ball	repeats sentence with 16 syllables
8		draws variety of people	picture stories are interpreted
	rides a bicycle		sentence constr. stabilized; future tense
7	Jumps at least 3 feet wide, 1 foot high		reads short text
6½	walks backward on toes	ties bows, shoestrings	retelling possible
		throws ball further than 3 y	learns characters
6	Roller-skating	draws 6-part man	
		eats with knife and fork	
5½	goes forward on toes	copies square	
		uses knife for cutting bread	repeats sentence of 10 syllables
5	uses a swing by him(her)self safely	draws 3-part man	learns simple verses
			puns; creates own words
4½	climbs ladder	catches bouncing ball	
			asks for meaning («why»)
			repeats sentence of 8 syllables
4	jumps on one leg	able to button	uses names and surnames
		safe sequence of movements	uses childrens' songs
		threads perls on to string	asks «why?», «how?»
3½	goes down stairs	catches rolling ball	uses «J»-form
		copies round shapes	vocabulary more than 200 words
	drives on tricycle or quadricycle		repeats sentence of 6 syllables
3	jumps with two legs	puts shapes into the proper holes	uses plural
			forms sentences of 3 words
		builds tower with 4 bricks	asks «where?», «who?», «what?»
2½	goes up stairs with-out holding to railing	builds bridge of 3 parts	asks about names and things
			eats by him(her)self
	stable balance		
2		scribbles upon his(her) own initiative	forms «sentences» of 2 words
	pushes ball with foot	uses spoon safely	eats «normal» food
	goes up stairs while holding on to railing	able to decant liquids	points to named parts of the body
			uses 2–8 words
1½	goes also backward	uses spoon, insecure	imitates noises
	walks without help	builds tower from 2 parts	repeats simple words
	walks with support		reacts to simple request
	stands freely	grips with thumb and index finger	chews; takes coarse food
1	stands with support	handles building blocks	says «Mom» specificly to mother
	crawls forward and backward	points with hand or finger	drinks from cup
	creeps forward	reaches for, holds toy; cannot let it go	
9/12	sits without aid for a long time	grabs threads	says «Mom», undirected
	sits for a short while without aid	able to hold two toys	bites off biscuit
	supports him(her)self on hands	changes toys from one hand to the other	
6/12	lets him(her)self be pulled up for sitting	turns toy between hands	forms syllable chains
	turns body from dorsal to abdominal pos.	targeted individual movements	laughs sonantly
	supports him(her)self on arms	tries to grab toys	takes pap from spoon
3/12	holds head upright for at least 30 seconds	holds rattle in hand	squeaks, chatting
	holds head upright for at least 5 seconds	untargeted complex movements	screaming stage
	turns head to side		

Name, Surname: Birth date:

Fig 263: Developmental Analysis.

SOCIAL DEVELOPMENT	INTELLECT. PERFORMANCE; IDENTIFICATION; UTILIZATION; COMBINATION	SPECIAL DATA ON INDIVIDUAL DEVELOPMENT	Age
is able to exercise self-criticism	explains terms		14
criticizes others	repeats 6 figures		13
discovers its own «self»	indicates the opposite		12
	interest in legends, technics		11
ancious to have pals	masters figures up to 100		10
team games	recognizes nonsensicalness		
thinking in terms of rank	explains pictures		9
	identifies shapes in the maze of signs		
	describes a picture		8
efforts to perform are identifiable	repeats 4 figures		
is conscious of his(her) duty	distinguishes between right and left		7
ties bows, laces			6½
	interest in fairytales		6
constructive common games	knows all basic colours		
combs his (her) hair	recognizes shortcomings, deficiencies		5½
strong feeling for family	knows meaning of «1–4»		
sex-specific game	has scale for sizes and quantities		5
makes friends	names 3 colours		
cleans teeth	relates experiences		
first signs of competitive feeling	constant memory		4½
observes rules of game	knows meaning of figure 3		4
is dependable, clean and dry			
	brings 3 objects upon request		
	knows 3 basic colours		3½
able to dress and undress	repeats 3 figures		
able to dress of			
goes to the bath-room by him(Her)self	distinguishes between front and back		3
plays with other children	recites simple nursery rhymes		
plays for a long time	assigns the proper colours to each other		
wants to do a lot by him(her)self	recognition stays for months		
plays games with assigned parts	repeats 2 figures		2½
	differentiates between «a lot» and «a little»		
reacts logically to situation	matches simple figures		
dry during the day	differentiates «round», «square»		2
expresses wishes			
is potty trained (stool)	differentiates «top», «bottom»		
	differentiates «large», «small»		
follows simple commands			1½
gives toys up	reacts to names		
rolls ball to the mother	points to familiar objects		
calls, when wet	recognition lasts 2 weeks		
resistance, when mother leaves	understands simple words		1
waves «bye, bye»	reacts to light colors	The data are so timed, that 90% of children with normal development are capable of these functions. The aproximate logarithmic orientation symbolises rate (tempo) of development. Developmental manquos are immediatly visible. The time of testing will be signed by a (colored) horizontal line. The criteria below this line are noted in the same color in the squares to the right.	
fetches toys			9/12
helpes to hold cup	recognition lasts hours		
recognises people as unfamiliar	turns head to sources of noises		
imitates simple movements	differentiates kind and stem voices		6/12
shows contact-pleasure	listens to music		
interest for toys	looks to toys, when removed		
answers smile by smiling	follows light	■ total ability ⊡ unsure □ inability	3/12
visual contact with mother	reacts to noises		

ed, that is the earlier the evident growth phase of the human brain is utilized, (the first 4 years of life).

B) Implantations by injection should always be incorporated into an wholistic medical concept of medicamentous, pedagogical and training methods.

C) Implantations should be continued as long as substantiated progress can be registered.

Special Indications

The effect of «cell therapy» depends on the basic condition, age and the wholistic therapeutic concept. The following possibilities and limitations result for various disturbances of the central nervous system:

Congenital Metabolic Disorders

They represent a highly diversified field of more than hundred, partly very rare, illnesses. As a rule, enzyme defects are at the base of these diseases of the metabolism; before the enzymatic step, substrates are dammed up and tissues damaged. Tissues with a high degree of metabolic turnover such as liver, brain, cardiac muscle, are affected usually more frequently and more seriously than tissues having a smaller metabolic turnover. Tab. 31 gives a survey of the important innate metabolic disturbances.

Up to this day it has not been possible to make special recommendations for the application of implantations by injection for innate disturbances of the metabolism because only individual observations relating to rather few disturbances of the metabolism have become known.

The following tissues seem to occupy a central position in implantation therapy: liver, mesenchyme, suprarenal gland, placenta.

With innate or acquired immuno-deficiency (antibody deficiency, syndromes) the use of thymus, bone marrow, liver and mesenchyme is recommended.

Infantile Cerebral Paresis

A classification of the types and subdivisions of infantile paresis can be seen from Tab. 35.

The age limit of the 4th year of life is particularly important for the use of cell therapy in the case of a cerebral paresis. The later cell therapy is applied in addition to the other methods in the first 4 years, the lesser the success will be.

The following is worth mentioning with regard to the various types: In spastic types, a spastic condition fixed once and not influenceable to a noteworthy extent by gymnastics, cannot be influenced by cell therapy methods beyond the 4th year of life. What can be done is to improve the biological overall condition of the children and the mental functional capacity. Compared with this relatively small responsiveness in the cases of fixed spastic types, effects can be achieved with the dyskinetic forms (choreoathetosis) and the atactic forms up to the time beyond the first decade of life though they are smaller than in earlier stages of life.

For the *spastic forms* the following materials are used: cerebral cortex preparations, cerebrum hemisphere, thalamus, midbrain, cerebellum, spinal marrow.

For the *dyskinetic forms* the emphasis of therapeutic application is on the diencephalon, basal ganglia, hypothalamus, thalamus, temporal brain, and cerebellum.

For the *hypotonic types* of infantile cerebral paresis,mainly fetal spinal mar-

row, occipital brain, cerebellum and midbrain should be used.

Atactic types originating, in the cerebellum or in the spinal marrow should primarily be treated with spinal marrow, cerebellum, midbrain and, possibly, occipital brain.

Heredo-degenerative conditions of the central nervous system present a diversified field of rare types of diseases which, up to this day the therapeutic experiences and observation-times are limited (see special chapter).

The application of fetal cerebral tissue in previous years has shown that no effects on a progressive development or even a healing process in these diseases can be achieved; on the contrary, in individual instances fever reactions developed after implantation. This was proof that also fetal tissue is not tolerated well with most of these degenerative conditions, which, in part, are combined with an autoimmunisation process.

Only the administration of fetal liver, placenta, suprarenal glands, in connection with a subsequent specific enzyme therapy, has opened up trends promising for the future, even if a binding judgment of the final value cannot yet be passed. Considering the otherwise usually poor prognoses and the inescapable progressive development it is recommended, however, to try this therapy.

Enzyme Therapy

Enzymes are synthesis products of the cell organelles; as to their action they are catalytically active proteins. Numerous enzymes are made available to the organism of the recipient through the injection implantations of fetal tissues applied to specific organs. Unlike biochemical substrates, however, their action is only short, because they are rapidly utilized and transformed. According to the logical consequence of this reality it is advisable to maintain the introductory catalysis by a prolonged application of enzyme preparations. Parenterally administered enzymes are governed by the same laws of action as substrates; they penetrate into the cells where they are lacking or are present in reduced quantities; a local need, a cellular insufficiency is the premise for effectiveness. The live cell behaves toward enzymes the same way as toward vitamins, minerals, amino-acids, peptides and other substances.

The selection of enzyme preparations that can be used unter the therapy concepts for mental retardation is still incomplete. The application presents problems.

For many degenerative disorders of the central nervous system digestive enzymes are indicated.

What is available in sugar-coated pill form are the following: *Wobe-enzym-Tabl.®*; as enema tablets: *Wobe-Mugos Klistier-Tabletten®*; as soluble preparations administered subcutaneously or as preparations of Enzypharma in ampoules, which can be administered via the mucous membrane of the mouth. The following preparations among them are of importance for the disturbances of the central nervous system:

Aminosäure-Komplex®

contains ligases of the Amino-Acyl-Ribonucleic acid synthesis.

Coliacron®

suitable for diseases of the neurohormonal system and applicable to hypotonic forms and general weakness of connective tissue; it contains the following active substances:

Symptom	Age / Years: 0	2	4	6	8	10	1	3	6	9	2	3	4	5	6	7	8	9	10	11	12	13	14
Intelligence normal																							
Debility																							
Imbecility																							
Idiocy																							
normocephalic																							
makrocephalic																							
mikrocephalic																							
Monoplegia																							
Diplegia																							
Hemiplegia																							
Triplegia																							
Tetraplegia																							
Contractures																							
Rigor																							
Muscle-Hypertonia																							
Muscle-Hypotonia																							
Dystonia (alternat. Tonus)																							
Convulsions																							
Hyperkinesia																							
Coordination-Disorders																							
Tremor																							
Chorea																							
Athetosis																							
Restlessnes																							
Eretism																							
Autism																							
extrapyramidal Symptoms																							
Initiative-Disorder																							
Concentration-Weakness																							
Emotional Incontinentia																							
Perseveration																							
Legasthenia																							
Polydipsia																							
Polyphagia																							
Hypertrichosis																							
Vegetative Disorders																							
Trophic Disorders																							
Lability of temperature																							
Hypersensibity																							
Hyposensibility																							
Hyperhydrosis																							
Anhydrosis																							
Ataxia																							
Strabism																							
Eye-Paresis																							
Nystagmus																							
Reduced Visual-Capacity																							
Amaurosis																							
Reduced Hearing-Capacity																							
Deafness																							
Dyslalia																							
Swallow-Disorder																							

For use: Symptome complete ■ partial ☒ abortive ⊡

Fig. 264: Documentation of the neurological symptoms.

(i. u. = international units)

Succinate-dehydrogenase	8 i. u.
NAD-kinase	8 i. u.
Acetyl-CoA-synthetase	6 i. u.
Glutamin synthetase	6 i. u.

Rheumajecta®

for mesenchymal metabolic disorders
contains:

Sulfate-adenyl-transferase	2 i. u.
Chondroitin-sulfo-transferase	2 i. u.
Cholinacetyl transferase	$3\frac{1}{2}$ i. u.
Katalyse: hydrogenperoxyde-oxydo-reductase	$6\frac{2}{3}$ i. u.

Oculucidon®

for building up mucopolysaccharides, usable for mucopolysaccharidoses and eye conditions
contains:

Hexokinase	6 i. u.
Glucosamin-kinase	6 i. u.
Glucosamin-acetyl transferase	2 i. u.
Sulfate-adenyl transferase	50 i. u.
Chondroitin sulfo-transferase	50 i. u.

Hydrolysates

The biological components for diseases of the central nervous system are supplemented by hydrolysates. Here the most comprehensive experience pertains to the raising of prematurely born children, the apallic syndrome and psychic diseases treated with the preparation Cerebrolysin®. This preparation may be used for injection and for permanent infusions.

Ultrafiltrates

Cell-free ultrafiltrates as oral preparations are used

as brainfiltrates for brain disorders
as liver-placenta-pancreas-intestine filtrates for degenerative disorders of the central nervous system, muscles and metabolic diseases,
as cartilage-bone filtrates for innate and degenerative bone diseases,
as thymus-spleen filtrates for immundeficiencies.