Chromosomal abnormalities

The structural aberrations of chromosomes use to be subdivided by groups into abnormalities of the autosomes and gonosomes (sex-chromosomes), on the one hand, and by disorders of distribution, on the other hand. One speaks of monosomies (1 chromosome instead of 2), trisomies (3 instead of 2), translocations (displacements of chromosome mass) and deletions (injuries to chromosome constituents without numerical aberration or displacement of material). Tab. 23 contains a survey of the clinically most important forms.

Sufficient therapeutic experience with this group of disorders is available only for Down's syndrome and Turner's syndrome. For all other chromosome abnormalities, sporadic cases make, at best, rough outlines for a consistent therapy. The treatment has to rely on the symptoms of clinical results rather than on the findings as to chromosomes, and must be conceived for the entire medicine (fig. 229, 230, 231). Some succerr promises aberrations of the chromosomes Nr. 9, 10, 11; in trisomy 13 und 18 we have no celltherapeutic experience till now.

Tab. 23: **Aberrations of chromosomes**

1. Translocation on chromosome 1
2. Wolf-Hirschhorn-Syndrom (Deletion chrom. 4)
3. Syndrome of deficiency on the short arms of chromosome 4
4. Cat's-cry syndrome (abnormality of chromosome 5)
5. Monosomy 9
6. Partial Trisomy 10 q
7. Trisomy 13–15 (Patau's syndrome)
8. Trisomy 18 (Edwards' syndrome)
9. Deletion chromosom 18 (DE GROUCHY-S.)
10. Trisomy 21 (Down's syndrome)
    a) free trisomy 21
    b) mosaic mongolism
    c) translocation mongolism
    d) double-trisomy (48 chromosomes)
11. Rare aberrations

Abnormalities of the sex chromosomes

1. monosomy X (45,X)
2. polysomias
    a) triple-X-syndrome
    b) tetrasomy X
    c) pentasomy X
3. XY-polysomias
    a) Klinefelter-syndrome (XXY-type, 47,XXY
    b)XX-type (46, XX)
    c) XXXY-type (48, XXXY)
    d) XXXXY-type (49, XXXXY); Fraccaro-type
    e) 49, XXXYY und 49 XXYYY
    f) XXYY-type (Double male)
4. gonosomal mosaics

Down's syndrome

Down's syndrome (= mongolism, mongolism-syndrome, mongoloidism, trisomy 21, trisomy G) is the most frequent and most important innate disorder accompanied by chromosomal abnormalities. From the correlation of the clinical symptoms to certain (not uniform) chromosomal aberrations (trisomy 21, translocations, mosaicisms) it is often concluded that the symptoms occurring in the course of development are fatal and inevitable. This resignative interpretation

Fig. 229:
Translocation on chromosome 1
A boy of 5 years is admitted for considerable retardation of his development. He used only fragments of syllables, is little concentrated, cannot be brought to work, appears inconstant. Microcephaly, head of 47.5 cm (−4 cm) in circumference, with hypoplastic frontal and temporal parts of the forebrain. Dysmorphy in the upper head-somite including ears and eyes.
After the first implantation already (Apr. 26, 1977: 100 mg of diencephalic lyophilisate, 100 mg of cerebral hemisphere, 150 mg of placenta male fetus), distinct improvements of speech, of sociability and initiative were obtained. After 4 series of implantations at the age of 6 10/12 years (May 1979), the rough movements and sociability nearly correspond to the age and vocabulary of the 2-year-old with certain achievements adequate to the 3rd and 4th years. Circumference of head: 48.6 cm.

Fig. 230:
Cat's-cry syndrome
Even repeated implantations of fet. brain tissues improve just slightly the general condition and microcephaly.

Fig. 231:
Dysmorphy syndrome in monosomia 9.
As a new-born many signs of dysmorphy: hypertelorism, small eyes, deep ears, shield-breast, defect of diaphragm, displacements of body-proportions, nail-hypoplasia and contractures of all joints, only the hands were opened.
At the age of 8/12 years muscular hypotony, no static functions. Learns to be seated at age of 10 months, six weeks after first implantation of 100 mg of diencephalon and 100 mg of cerebrum, learns to walk freely at 2 years, uses 10 words.

of morphological findings on a subcellular level has done immense damage to generations of afflicted children and parents.

In contrast to this nihilism palliated with the term «present state of science» there have been for 30 years a medical practice and experience proving not only scientifically but also biologically on a generation of mongoloids that Down's syndrome can be influenced. Among the pioneers of this evolutions are HAUBOLD H. (1954–1967); GOLDSTEIN H. (1956, 1959); FAHLISCH K. (1961); MOMMSEN H. (1955–1959); FELDMANN H. (1959, 1979, 1982); SCHUBERT E. v. (1957); SCHOLZ K. (1973, 1974); HALLER B. (1970–1980); ZELLER W. (1957).

The author's own experience covering more than 25 years relies on 1780 long-term observations documented and evaluated under various biometrical, metabolic and therapeutic parameters. The plan of therapy adjusted to all sections of medicine based on these extensive studies and fixed in individual publications between 1953 and 1983 will be explained more at length as example of other innate syndromes in order to work out the interplay of the various treatments (see fig. 232).

Conception of treatment

In contrast to the present conformistic conception that trisomy is the cause of Down's syndrome, the following representations are based on other fundamental ideas and biologico-clinical facts. They relate to the biological central question whether the function makes the structure or whether the structure determines the function. Applied to the processes of germ-cell fusion and to the first processes of division, the following questions arise:

- Is there a primary lower functional valence of the germ-cells leading to abnormal processes of division and fusion in the chromosomes, which provoke a secondary influence on the abnormal forms?
- Is the morphological aberration of the chromosomes really the primary noxa from which all other symptoms can be derived?

The abnormalities of chromosomes confirm the correlation with the clinical symptoms of Down's syndrome, not however their causal importance. The aberrations of chromosomes are probably the consequence of an additional pathogenous principle in the function of the germ-cells, which come into question to be the cause only because they can be identified optically and morphologically. Clinically, this alternative implies the question whether the metabolic aberrations in children suffering from Down's syndrome are the result or the cause of the chromosomal abnormalities.

Important facts speak for the conception that Down's syndrome is a disease correctible in essential partial symptoms rather than a fatal consequence of chromosomal-morphological aberrations.

Therapeutic requirements

Down's syndrome is a disorder affecting the form and function of the entire or ganism, and therefore its symptoms consist of pathological abnormalities (form variants) and functional aberrations. The progredient retardation in untreated mongoloids is the outcome of the dysfunctions, the common denominator of which seems to be a metabolic disturbance in all cellular membranes. This disturbance influences metabolic, rapidly growing tissues (brain, glands of the internal secretion, cartilage, liver, immunocytes) more than metabolic less active tissues.

Table 24: **Response to therapy of important symptoms seen in Down's Syndrome**

Removable	Improvable	No Response
Saddle Nose	Hypertelorism	Brushfield Spots
Narrow Palpebral Fissures	Epicanthic Folds	Milk Dentition Anomalies
Eye axis	Mongolian Eye Axis	Broad Upper Part of Ilium
Squint	Nystagmus	Pseudoepiphysis
Conjunctivitis	Abnormal Ear Formation	Synostosis
Blepharitis	Secondary Dentition Anomalies	Chromosomal Abnormalities
Macroglossia	Abnormal Behaviour	Pterygium
Brittle Hair	Flat Acetabulum	Ape Furrow
Obstipation	Coxa valga	«Sandal» Furrow
Microcephalia	Brachymelia	Dermatoglyphics
Hypognathism	Brachycarpia	Non-Operable Heart Diseases
Weakness of Ligaments	Clinodactylia	
Muscular Hypoplasia	Cheilosis	
Muscular Hypotonia	Hypogenitalismus	
Umbilical Hernia	Social Development	
Inguinal Hernia	Motor/Kinesthetic Development	
Retarded Ossification	Speech	
Osteoporosis	Mental Development	
Lowered Resistance to Infection	Physiognomy	
Thickened Skin	Stature	
Cervical Lipomatosis	Abstract Process of Thought	
Operable Heart Diseases		

The Down syndrome is a multiple handicap which concerns both the

Physical development

a) anthropometrically (insufficient growth, dislocation of proportionate ratios, microcephaly, physiognomy);
b) statomotorically (delay of the statomotoric development, disorders of the fine motorial and coordination systems)

and the

Mental development

a) in the psychic and social areas;
b) in the intellectual sphere.

In addition, there is a general weakness of the defense system against infections.

Inevitably a «multiple handicap» results in the need for multidimensional care.

Numerous experiments made in the past failed because they were structured in terms of too narrow a concept; they did damage to the Down children – not on account of the method of treatment applied but by the fact that further therapeutic requirements were neglected.

Not only a 3-decade experience and the success obtained in this field speak for considering Down's syndrome a treatable disease needing a therapy, but also a number of exact facts:

1. *The somatic, stato-motoric, intellectual and psychic developments* decline with the advancing age gradually in relation to the norm of age. Many symptoms distinctive of the fate and position of these children in the society are not original but develop *secondarily* in the course of growth.
2. Many symptoms, primarily not marked but manifesting in the course of growth, are possible only with a participation of the *endocrine system* (nanism, hypothyreosis, symptoms of adrenal insufficiency).
3. The *aberrations of proportions and growth of the brain skull and facial bones* are little marked at birth and in the first months of life, in part they do not exist. The objective measurements are mostly still within the norm, about the mean value. With advancing age, the growth of the cranium lags behind the norm; the brain is not equal afflicted because the occipital and parietal regions stay behind most. The first anatomic changes are found in the cerebellum.
4. While the growth of the brain is retarded, the *mongoloid physiognomy* becomes more evident as the deformation of the cranium and facial bones continues with the advancing age unless a therapeutic intervention is initiated.
5. Owing to the general *underdevelopment of the mesenchyme*, the weakness of the defense against infection adds much to impair the children's development.
6. There is no direct relation between the findings of chromosomes, the clinical symptoms and the intellectual development. This lack of correlation is most evident in mosaic-like mongolism as a varying percentage of body-cells and tissues show a normal structure of chromosomes.
7. The *nanism* of mongoloid children begins during infancy and reaches the peak in the last puberal stage of

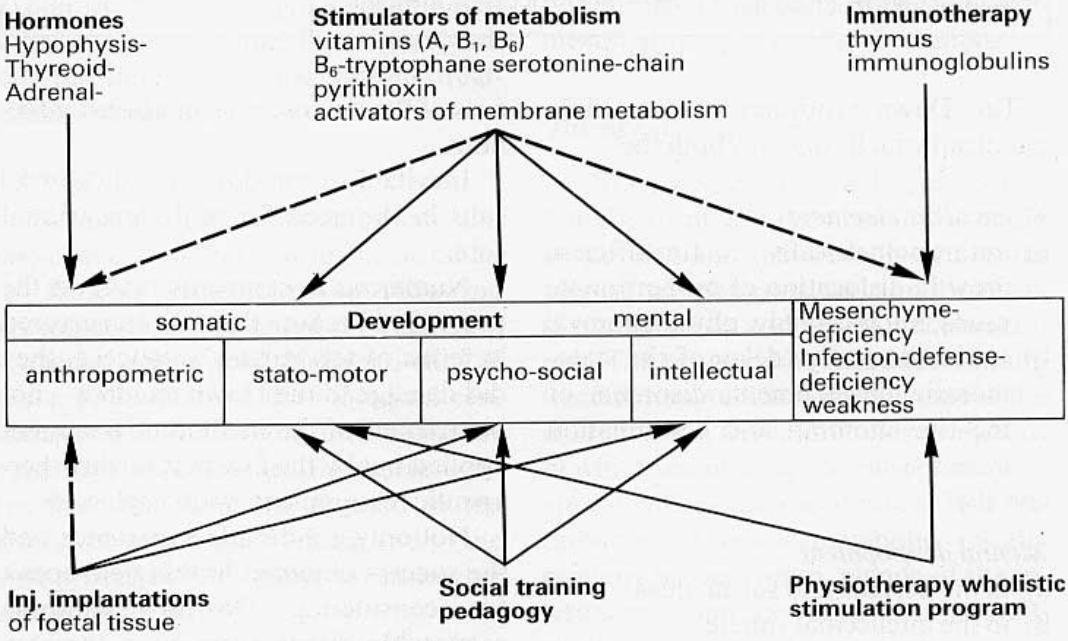


Fig. 232: Therapies for Down's syndrome (see text)

growth. The regularities relying on a long-term observation of mongoloid children seem to suggest a continued *deficit of the puberal phase of growth*, which consequently determines much the dimensions of reduced body length.

Therapeutic postulations

If the practical assessment of the mongoloid syndrome is considered to rely on the fact that here a disease with a progressive retardation of the development is in question, the following therapeutic postulations result:

1. To *regulate the balance of the endocrine glands* in such a way as to reduce or to stop the endocrine deficits.
2. To reduce or to stop the progressive deficit of the *brain growth.*
3. To treat the lowered *resistance to infection.*
4. To remedy the *weakness of the connective and supporting tissues.*
5. To *prevent the deprivation* elicited by therapeutic resignation as an additonal injury to the children.
6. To develop and to use consistently a *pedagogy* adjusted to the outcome obtained.

Consequently, the therapy must aim at all symptoms and groups of symptoms to influence. The following methods are available:

a) hormones
b) stimulators of metabolism
c) immunotherapy
d) implantations by injection
e) social training and pedagogy
f) medico-gymnastic treatment of the whole body (stimulation program)
g) speech therapy.

Therapeutic principles

An analysis of the situation will show first that all developmental sectors are afflicted, most however the intellectual development. Nanism, microcephaly, disturbed proportions of the body stature, timely and formal abnormalities of ripening are distinctive of the anthropometric component of the somatic development whereas the retarded statomotor development characterizes its functional component. Within the mental sphere, the social development (including the retarded learning of social functions up to antisocialism) is affected just as well as the intellect, which shows the most serious deficiencies in the area of abstract thinking. The therapies are illustrated synoptically in fig. 232.

Metabolic therapy

The literature on metabolic aberrations in Down's syndrome provide only in certain areas binding conclusions on therapeutic consequences. Among them are:

a) disturbed absorption caused by reduced enzyme activities in the intestinal secretion;
b) demand for vitamin A as an expression of reduced protection of surfaces;
c) disturbed metabolism of vitamin B1 and vitamin B6 in connection with the restricted metabolism of tryptophane;
d) abnormalities of the tryptophane metabolism, which entail a lowered serotonin level;
e) cytochemical indications to transport disturbances in the cytomembranes;
f) progressive hyperuricaemia;
g) low taurin levels;
h) aberrations of the calcium-magnesium levels;
i) high phosphate values;

j) low intracellular zinc values, potassium-, manganese-selen-values (hair);
k) high transferrin values;
l) low to reduced serum-iron values;
m) enzymatic aberrations;
n) disorders (insufficiencies) in the immunglobulin-synthesis.

Of importance for the therapy are medicaments of metabolic intermediate stages, vitamins and diet recommendations.

Vitamins A, B1 and B6 need continuous substitution; the minimum dose must come up to the daily requirement. If there are symptoms of lacking vitamin B (perléche, cheilosis, lingua scrotalis, chron. conjunctivitis, branny skin, seborrhoic hair-bed), vitamin B1 ought to be increased to 50–150 mg/die. Vitamin C should not be administered by quantities above average, vitamin D by as far as possible small doses; several multivitamin products cover these requirements.

The vitamins of the B-group – which occupy a central position in the entire pathological process of Down's syndrome (SCHMID, REHM and CHRISTOFFER, 1974; READING CH. M., MCLEAY, A. a. NOBILE S., 1979) – intervene in the tryptophane metabolism at six sites. Here is also the point of attack for the pyrithioxin (Encephabol®), a vitamin B6 derivative without the character of a vitamin, which influences specially the development of speech in infancy. The tolerance of pyrithioxin is comparatively low in eretic children; sometimes they do not even tolerate a teaspoonful daily of it. B-vitamins are to raise above all the serotonin level lowered in the mongoloids.

Nutrition

Food may replace many of the mentioned medications. It is easier to make this statement in theory than realizing it in practice, because extensive preservation of basic food items creates a situation in which even an interested doctor is no longer able to clearly recognize the nutritional implications.

The basis for the nutrition of Down children should be a full-value normal diet cutting down on the amount of carbohydrates. The majority of Down children instinctively rejects merchandise containing sugar (candies). This diet should include adequate bread – rye bread, leavened bread, whole-wheat bread – an anbundant amount of salads, raw vegetables and fruit. Salads which are in the stage of transition from the yellow to the green colour, contain particularly many B vitamins.

The daily amount of milk should not exceed the equivalent of 500 ml whole milk because of the calcium supply connected with it. To support the maturation of the medulla a weekly amount of 2–3 beaten eggs or egg yolk is recommended. As far as feasible the addition of small amounts (2–3 tablespoonfuls) of raw brain of young animals, mixed in a Starmix blender, for soups, vegetables, puddings or milk drinks has proven advantageous. From the second half-year on, the objective should be 1 to 2 meals of sea fish weekly.

With selective deficiencies in individual elements and trace elements the following recommendations may provide some help:

Potassium deficiencies can be corrected through diet by giving the child food which is rich in potassium, such as potatoes, carrots, peaches, apricots. For cases of selenium deficiency the best source of selenium is brewer's yeast or other kinds of yeast.

Manganese deficiency is widespread due to the consumption of bleached flour and baked goods; the best substi-

Tab. 25: **Basic therapy for Down's syndrome**
Ground schemes

A. Babies up to 3rd month of age

Rp. *Astrumin*
S. Mo., Wed., Fr. 1 tabl.
2. *Multibionta drops*
S. 20 drops daily
3. *Membravit*
S. 1 tabl. daily
4. *Encephabol juice*
S. 1/2 meas-spoon daily
5. *Pancreon*
S. 1 tabl. daily

Rp. *Thyreoid dispert 0,1*
S. Mo., Fr. 1/2 (till 1) tabl.
2. *Astrumin*
S. Wed., Sat. 1 tabl.
3. *Multibionta-Tropfen*
S. 30 drops daily
4. *Membravit*
S. 1 tabl. daily
5. *Nootrop (or Normabrain) 800*
S. 1/4 tabl. daily

B. Babies from 4–12 months

Rp. *Thyreoid dispert 0,1*
S. Mo., Wed., Fr. 1 tabl.
2. *Multibionta*
S. 30 drops daily
3. *Membravit*
S. 1 tabl. daily
4. *Encephabol juice*
S. 1 tea-spoon daily
5. *Normabrain juice*
S. 1/2 meas-spoon daily

Rp. *Thyreoid dispert 0,1*
S. Mo., Fr. 1 tabl.
2. *Astrumin*
S. Tu., Th., Sat. 1 tabl.
3. *Membravit*
S. 1 tabl. daily
4. *Mulgatol-Gelee*
S. 2 teespoon full daily
5. *Indovert-Juice*
S. 2 teespoon full daily

C. Infants 2–5 years

Rp. *Thyreoid dispert 0,1*
S. Mo., Wed., Fr. Sat. 1 tabl.
2. *Mulgatol jelly*
S. 2 tea-spoons
3. *Membravit*
S. 2 tabl. daily
4. *Neurotrat*
S. 1 bean daily

Rp. *Thyreoid dispert 0,3*
S. Mo., Wed., Fr. 1/2 tabl.
2. *Astrumin*
S. Tu., Sat. 1 tabl.
3. *Membravit*
S. 1 tabl. daily
4. *Indovert-Juice*
S. 2 teespoon full daily
5. *Vitafestal*
S. 1 tabl. daily in the evening

D. Children 6–12 years

Rp. *Thyreoid dispert 0,3*
S. Mo., Wed., Fr. 1/2 dr.
2. *Vitafestal-Drag.*
S. 1 dr. daily with dinner
3. *Membravit*
S. 2 tabl. daily
4. *Neurotrat forte*
S. 1 bean every 2nd day

Rp. *Thyreoid dispert 0,3*
S. Mo., Wed., Fr. 1/2 (till 1) tabl.
2. *Astrumin*
S. Tu., Th., Sa. 1 tabl.
3. *Membravit*
S. 1 tabl. daily
4. *Eunova*
S. 1 drop daily
5. *Neurotrat forte*
S. Mo., We., Fr. 1 tabl.

Suite of table page 216

Suite Tab. 25: **Basic therapy for Down's syndroms** Ground schemes

E. Older school-children and adolescents	*The substitution of thyroid preparations must be increased or reduced individually, according to the clinical symptoms. Integral preparations are better than single components T_3 or T_4. If available, a combined preparation of hypophysis and thyroid tissue should be preferred during the first 6 years. the demand for vitamin B_1 is very high i. e. between 100–150 mg per day.*
Rp. *Thyreoid dispert 0,3* S. Mo., Wed., Fr. Sat. 1/2 dr. 2. *Eunova* S. 1 dr. daily with dinner 3. *Membravit* S. 2 tabl. daily 4. *Neurotrat forte* S. 1 bean every 2nd day	

tute in the food is whole-meal flour and the corresponding kinds of bread.

Stays on the sea-shore of three to six weeks exert a favourable influence on mongoloid children; this is true especially for the inclination to infection but also for the statomotoric development in infancy. The spontaneous development of the mongoloid children growing up on the seashore proceeds usually more favourably than that of the children living in inland or montainous regions, according to the author's experience. The worst spontaneous development is seen in mongoloids of the chalky mountains (Swabian and Swiss Jura Mountains); they must be treated with more tracer-elements and hormones.

Enzyme therapy

Malfunction on the part of the digestive tracts (refusal to take food, diarrhea episodes, disposition for obstipation, abnormal gas formation, inflated belly) sometimes requires a substituting treatment with digestive ferments. With the exception of Pankreon® problems are created by a large volume of sugar-coated pills. For later childhood «Vitafestal» offers a suitable combination of digestive ferments and vitamins.

«Coliacron» , an injectable enzyme preparation, which may also be applied via the oral mucosa, provides unique help in serious muscular hypoplasias, muscular hypotonias and general weakness of the connective tissue. It is applied in series of 18–24 injections (2–3 injections weekly).

Up to the present the experience gained with Wobe-Mugos, Wobenzym, and *Ocolucidon* (mucopolysaccharide metabolism) are not sufficient. This sector of therapy has not been developed very much in the face of the numerous known anomalies of the enzyme metabolism of the Down syndrome. Also the relative high enzyme content of fetal tissue provided through injection-type implantations probably has a short-time effect only.

Endocrine substitution

With the Down syndrome the endocrine system is affected at different levels: diencephalon, hypothalamus, hypophysis, thyroid gland, suprarenal gland; gonades.

The neurocrine sphere is responsible for insufficient growth of the first years of life and probably also for acromicry.

The hypophysis commanding the glands of internal secretion is not an autonomous «control station» but depends, on its part, on the neurosecretory processes, especially on the «releasing factors» of the diencephalo-hypothalamic system (fig. 272–274).

A great deal has been written on the disturbances of the thyroid gland func-

tions, and there have been controversial discussions of the problem. None of the laboratory methods including the auto-antibody determination meets the re-uirement to provide guidance for a need of treatment. Relying on and waiting for positive reactions obtained with laboratory methods among young people and adults suffering from Down syndromes is not recommended; rather, guidance should be obtained from the chief clinical symptoms from the very beginning such as macroglossia, obstipation, hyperkeratosis, adynamia.

To simplify matters, the endocrine insufficiencies of Down's syndrome can be divided into two types i. e. the thyroid type and the diencephalic type. Hypothyroid symptoms prevail in the former, diencephalic symptoms in the latter (Tab. 24), and the symptoms become evident during the development in untreated mongoloids i. e. they do not exist primarily. These symptoms do not or just slightly develop in treated children.

The Function of the Gonades vitally influences the puberty features among Down children, its onset is early, among girls often as early as between the 8th and the 10th years; it is shortened in terms of time, and abortive as to the functional result. The «puberal growth thrust» effected through gonade hormones fails to develop or remains below the threshold values. In this growth stage the growth deficit is increased considerably.

Meantime the menarche age of mongoloid girls has come closer to the average population due to the multidimensional treatment described. Alone by including suprarenal glands and ovarium between the 5th and 8th years of life it was possible to increase the final height average of Down girls in the last five years to 151 cm (average height of untreated girls 142 cm); the height of those treated until 1975 was 146 cm.

The elimination of numerous organ preparations from the stock of medications is disadvantageous to the endocrine substituting therapy.

Complex correlations exist between Down's syndrome and the thyroid function. The therapeutic measures must conform to the clinical symptoms. Biochemical data are not reliable as a secondary dysfunction is in question. The doses will have to depend on the response of the symptoms (macroglossia, obstipation, husky voice, thickened skin, dry hair).

Ground schemes for the fundamental therapy with medicaments are contained in Tab. 25. The general rules should be adjusted to the individual requirements.

Mesenchyme insufficiency

The organismic weakness of the connective tissue (mesenchyme insufficiency) is of importance for the development of mongoloid children especially with respect to the following 2 points:

a) the stato-motoric development is inhibited purely mechanically by the hypoplasia of the supporting tissue (hypoplasia of the muscles, ligaments, tendans, vessels and skeleton);
b) the inadequate efficiency of the reticular and loose connective tissue impairs obviously the immunity against infection.

The inferiority of the supporting tissue can be influenced by gymnastic treatments of the whole body and by massage of the connective tissue; the parents should be given a program of physical exercises to carry out for ten to fifteen minutes twice or three times every day, in conformity with the actual state of the stato-motoric development. The gym-

nastics favour also the socialisation of the children.

Deficient immunity and defense against infection, biochemically identified by low rates of immunoglobulins, manifest themselves clinically by chronic and relapsing infections of the upper respiratory passages, enterocolitis during infancy, chronic rhinitis, tonsillitis, sinusitis, hypertrophy of adenoids, bronchitis and bronchopneumonia.

The defense against infection on the epithelial interface and the lymphatic zone of resistance can be improved by doses of thymus and multi-vitamins (vitamin A!). Moreover, antibiotics as well as inhalations and phytotherapeutics should be administered for short periods, further in certain cases tonsillectomy and adenotomy be performed to fight the chronic infections of the respiratory passages.

Besides the large and thick tongue, voluminous tonsils are an additional factor preventing the children from overcoming babbling and stammering because, mechanically alone, no articulation is possible.

Training therapy

The duty of training methods is to improve the functions of underdeveloped or damaged organs, organ systems or limbs by way of an increased stimulation with a specific objective. Passive stimulation aims at an active response to stimulation. In the case of multiple handicaps this training will cover both physical and mental activities. Transposed to the nerve system this means a stimulation at the periphery of the neuropils – that is at the motoric end-plates, axons, peripheral nerves – in order thereby to prepare the performance of functions up to the centre, the cell body of the neuron. Therefore, all methods of training are peripheral stimulation techniques with the aid of which the performance of the functions of the neurons shall be increased or established.

Methods of training are symptomatic treatment which should not be isolated in the therapeutic concept; rather, they must be embedded in a wholistic biological concept applied to the personality of the patient concerned. A maximum result will only be achieved within this framework.

The Down syndrome is a multiple handicap; under its therapeutic schedule numerous methods of training which start at the peripheral neuron will be applied in the course of development:

a) remedial gymnastics;
b) therapeutic gymnastics;
c) sports for the handicapped;
d) therapeutic swimming;
e) therapeutic horse riding;
f) motion therapy;
g) occupational therapy;
h) speech therapy (preparation of speech; training of speech motoricity);
i) optical training;
k) acoustic training;
l) music therapy;
m) behavioural therapy;
n) psychotherapy;
o) pedagogy.

It is not the purpose of the present analysis to give a valuation of these methods, which, indicated individually, may all have their advantages in specific stages of development. What should be avoided, is any monomaniac concentration.

Implantations by injection

Fetal tissue is implanted mainly to activate brain growth. This method, often incorrectly referred to as «fresh-cell therapy» is the most effective as it helps to remove certain symptoms resisting

Tab. 26: **Injection-implantations in Down's syndrome**

The succession and combination of organs given hereafter are based on statistical information on the growth of the size of the brain. They therefore relate, primarily, to the growth of the skull, the physiognomical changes and, connected therewith, to the social and intellectual development. This succession may be neglected in particular cases, according to individual symptoms or disorders.

As Down's syndrome affects also other organs (thymus, thyroid gland, adrenal gland, gonads, liver, kidney, etc.) and a general metabolic disturbance of cytomembranes is in question, it is advisable to include more tissues in the long-term plan of injection implantations.

For growth of the skull (brain)		Alternative or addition implants	
1. *Fet. mesencephalon*	100 mg	a) *weak resistance to infection*	
Fet. cerebral cortex	100 mg	thymus	100 mg
		adrenal gland	100 mg
2. *Fet. spinal medulla*	75 mg	b) *achondroplastic type (deep, broad root of nose, micromelia)*	
Fet. cerebellum	100 mg	cartilage	100 mg
		placenta	150 mg
3. *hypothalamus*	100 mg	c) *in considerable nanism, unless osteal (see b)*	
Fet. occipital brain	100 mg	comb. endocrine tissues (hypothalmus, thyroid, adrenal gland sex-spec. ovary, testes).	
4. *Fet. diencephalon*	100 mg	d) *6–10 years*	
Fet. cerebral hemisphere	100 mg	thyroid gland	100 mg
		fet. liver	150 mg
5. *Hypophysis sex. spec.*	80 mg	e) *in girls 6–10 years*	
Fet. temporal brain	100 mg	adrenal gland	100 mg
		ovary	120 mg
6. *Thalamus*	100 mg	f) *in boys 8–10 years*	
Fet. frontal brain	100 mg	diencephalon	100 mg
		adrenal gland male	100 mg
7. *Fet. basal ganglia*	50 mg	g) *in hyperuricaemia*	
Fet. parietal brain	100 mg	placenta	150 mg
		fet. kidney	100 mg
		h) *opacity of lens, vitreous body (early)*	
		placenta	150 mg
		lens	25 mg
		vitr. body	25 mg
		i) *in alopecia*	
		fet. diencephalon	100 mg
		adrenal gland	100 mg
		fet. liver	150 mg

This succession is repeated at intervals of 5–6 months in the first 6 years, of 6–9 months beyond the first 6 years of treatment unless the clinical symptomatology suggests other succession combinations or quantities.

medication and pedagogical measures. Authors sceptical about this method usually have no experience in this field or work with theoretically inadequate preparations (extracts chemically split up cellular derivatives, orally applied dilutions). The concept is to supply the body parenterally in a native biological form with the high outfit of substrates and enzymes of the rapidly growing fetal tissues.

If implantations by injection are made before the age of three years i. e. during the period of the most intense skull growth (= brain growth), progressive microcephalia with its concomitant physiognomical symptoms can much be prevented but merely be lessened beyond the age of three (Abb. 233, 234). After the fourteenth year of life, this method influences microcephalia just exceptionally, and hardly any effects can be expected for the physiognomy.

The implantations are performed by deep subcutaneous (epifascial) injection at five-month (four to six) intervals. If these specific implants are not chosen after the individual symptoms, the following succession is recommended (Tab. 26).

The results obtained so far relate to the given succession of implantations and quantities, and can probably be improved by augmenting the implants and including other tissues.

The mongoloid dyscephalia

The following remarks on the rules of growth in treated mongoloid children rely on the findings in untreated mongoloid children as defined in 1969. The 100 untreated mongoloid children statistically evaluated at that time are contained in the 200 cases of the present survey. The rules of the mongoloid dyscephalia will be treated concisely hereafter (SCHMID et al., 1969, 1972, 1982).

The abnormal development of the head as part of Down's syndrome comprises the formation of the cranium and facial bones as well as the changes of size, form and proportions. Whereas the abnormal development of the cranium is the outcome of the disturbed growth of the brain, the deformations of the facial bones result partly from mesenchymalossary and mechanical factors. The primary hypoplasia of the maxilla, which increases in the course of growth, combines with the consequences of macroglossy and of the adenoid vegetations.

The most important findings resulting from a biometrically founded craniometry shown on X-ray pictures of children suffering from Down's syndrome are:

1. The mongoloid dyscephalia is characterized by a brachymicrophalia increasing with the growth and a hypognatism of the superior maxilla.
2. The cranium, which represents the growth of the size of the brain, lies in the new-born mongoloid child usually within the tolerance of the norm; the microcephalia, therefore, is not innate in the majority of cases.
3. The growth of the cranium lags measurably behind the normal growth from the second trimenon of life; the deficit augments rapidly till the fourth year of life, later slows down gradually. The variation is essentially wider in girls than in boys.
4. The growth of the cranium (identical with the growth of the brain-size unless a hydrocephalus is in question) is not uniformly affected. The growth of the occipital, posterior parietal and temporal regions is much more retarded than the anterior parts of the skull.
5. Untreated, the mongolism develops at the end of the growth of brachysteno-microcephalia with a varying,

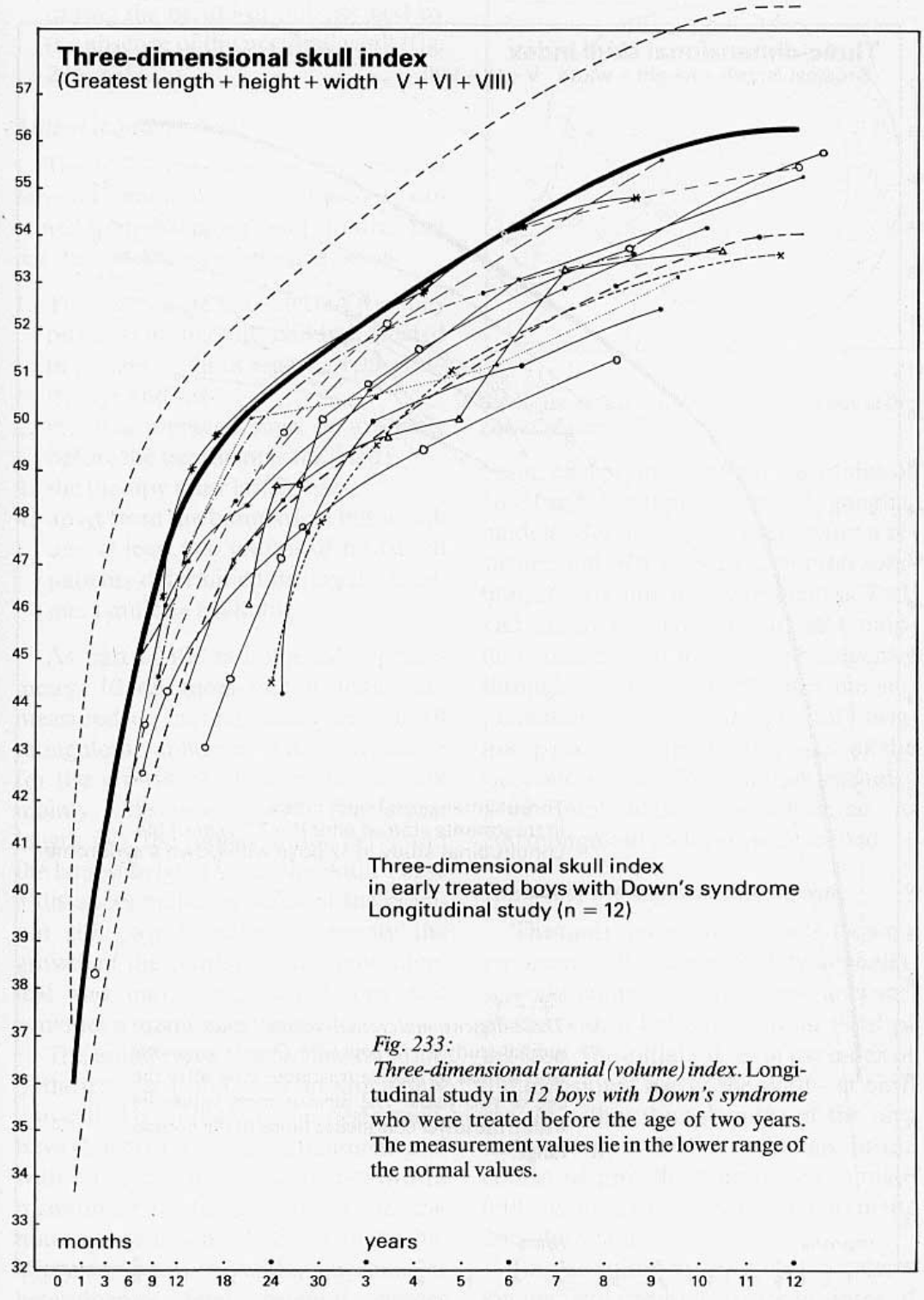


Fig. 233:
Three-dimensional cranial (volume) index. Longitudinal study in *12 boys with Down's syndrome* who were treated before the age of two years. The measurement values lie in the lower range of the normal values.

though, considerable in the majority of the cases, deficit in comparison with the normal average (fig. 235).

6. Further, the physiognomy is influenced by the changes of the facial bones. These are primary mesenchymal and not caused by the malformation of the brain. The reduced depth of

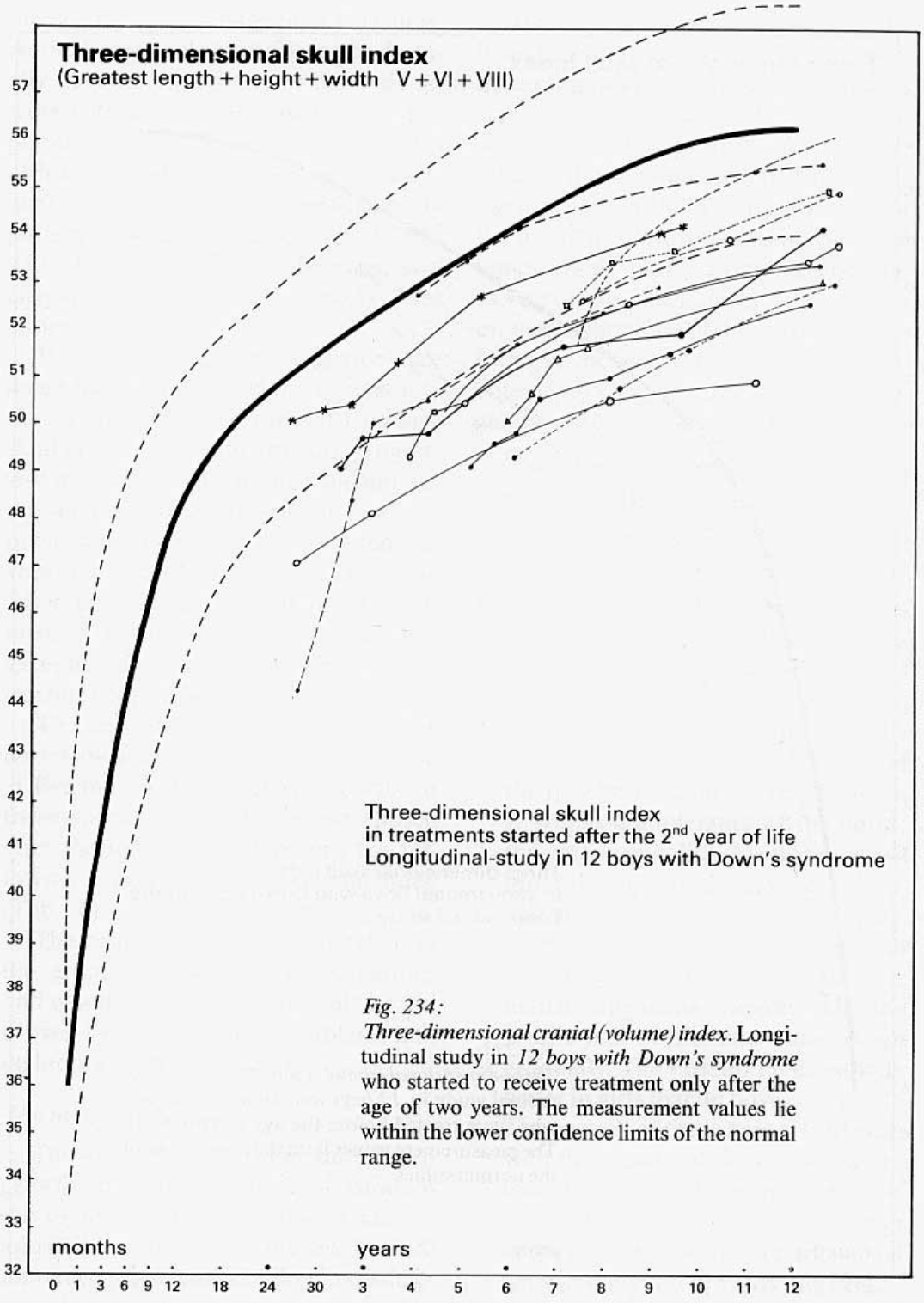


Fig. 234:
Three-dimensional cranial (volume) index. Longitudinal study in *12 boys with Down's syndrome* who started to receive treatment only after the age of two years. The measurement values lie within the lower confidence limits of the normal range.

the superior maxilla is there at birth and, together with the steep anterior cranial fossa, constitutes the typical mongoloid face. The central third of the face is flat to sunken and thus looks broad; these disproportions are still accentuated by the relatively normal growth of the inferior maxilla

during the period of puberty and by the absence of the occipital vault (fig. 235, 236).

Material and methods

The following biostatistical analyses rely on craniometric evaluations obtained from 200 mongoloid children under the conditions mentioned below:

1. The cases were not selected i. e. they relate to mongoloid children treated in 2 years, without regard to the gravity, age and sex;
2. the measurements must be available before the treatment is initiated;
3. the therapy must last 2 years;
4. apart from the biometrical initial values, at least two groups of measured patients determined during the treatment must be available.

As part of the radiological cephalometry, 10 distances and 6 angles are measured on cranial radiograms of all mongoloid children. Of importance for the growth of the cranium size are mainly 3 distances namely the largest length (V), the largest width (VII) and the largest height (VI) of the skull. These 3 distances make an index of the cranium size, which reflects correctly the growth of the cranium under physiological and pathological conditions and provides a metric scheme.

The initial values before the initiation of the treatment and cases, in which only a so-called basic therapy was performed, have shown that without a treatment and with basic therapy an influence worth mentioning on the growth of the cranium size cannot be obtained. In the 200 analysed cases, therefore, implants of heterologous fetal cerebral tissues (sheep, calf) were injected.

These implantations are applied by subcutaneous (epifascial) injections. As a rule, 2 × 100 mg of various parts of the

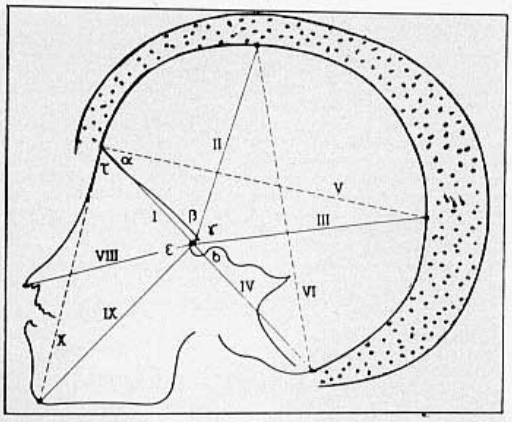


Fig. 235:
Skull-size deficit in untreated mongoloids at the end of growth.

brain, exceptionally minor quantities of 50–80 mg (hypophysis, basal ganglia, medulla oblongata) are used. After a resuspension in a Pannett-Compton solution, the volume of the implant is 7 ml, and another 3–4 ml of Pannett-Comptom solution are injected subsequently through the lying needle into the implantation depot. Used were only original packs of lyophilised tissues of the siccacell series. The analysis includes 1400 implantations administered to 200 mongoloid children as described.

Results of the implantation therapy

The most serious symptom to Down's syndrome is the mongoloid dyscephalia, a combination of brachy-steno microcephalia with a flattened central third of the face. The initial values of the index of 3-dimensional size of the skull – at birth mostly within the tolerance of the normal average – decline strikingly in the course of growth in untreated mongoloid children, with decisive deficits in the 2nd–4th years.

Implantations by injections of heterologous fetal cerebral tissues in doses of 2 × 100 mg and at intervals of 4–6 months normalize much the configuration of the cranium and improve the physiognomical conditions (fig. 235–243).

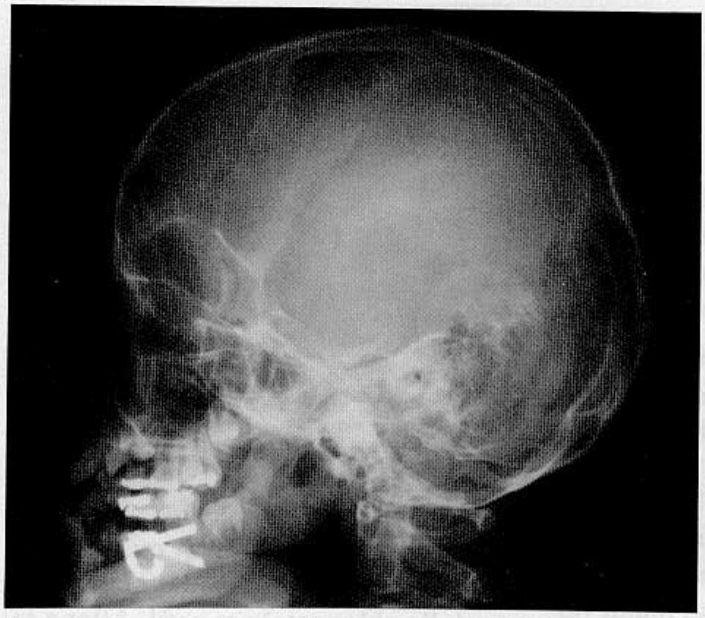


Fig. 236:
Brachymicrocephaly in a $9\frac{1}{2}$ year-old girl untreated so far. Flattening and asymmetry of occipital skull-vault, rough sella, hypoplasia of the middle face, high density of the cranial bone.

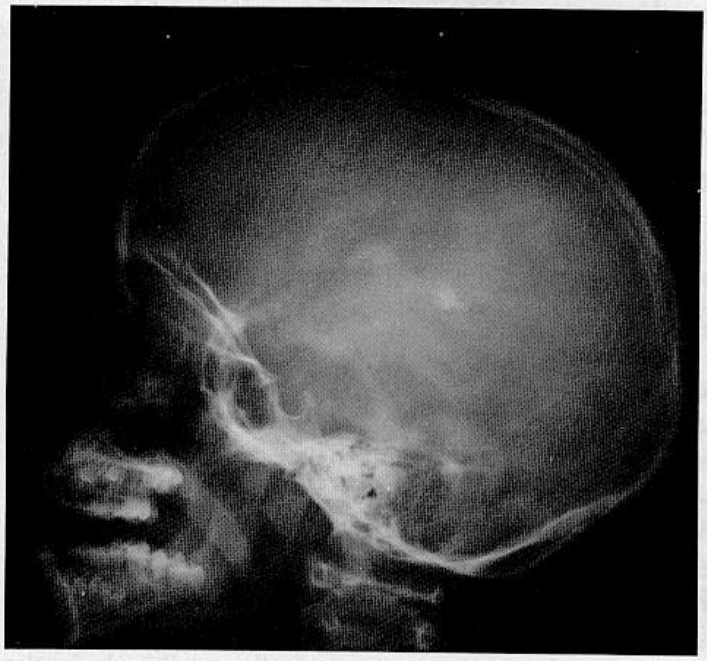


Fig. 237:
Cranial proportions in a 9-year-old mongol girl treated since early childhood. The cranial dimensions are slightly inferior to the normal figures, good relief of the cranium vault. Calcification of the plexus.
The children were compared because they came for the (first, repeated) examinations on the same day immediately one after the other.

The following principles result from the biostatistical evaluation of a prospective study on 200 non-selected mongoloid children before the treatment and after 2–3 implantations:

1. An increase of the cranial-size index can be obtained in about 2/3 of the cases treated.
2. The increase is not restricted to infancy and babyhood, as supposed formerly, but can be brought about also in the early years of school time.
3. The increase of the cranial-size index depends gradually on the initial situation; in other words: the greater the deficit of the size of the cranium at the

Tab. 27: **Effect of various tissular combinations on the growth of the skull size in 761 implantations**

Sex, age, initial situation and succession of implantations are not taken into consideration in this summation (with negative values subtracted).

Combinations of tissues		increase of volume index
cerebral hemisphere	+ mesencephalon	54,3 %
	+ diencephalon	54,3 %
	+ hypothalamus	54,3 %
	+ hypophysis	36,1 %
	+ frontal brain	36,1 %
cerebral cortex	+ hypophysis	49 %
	+ diencephalon	41,8 %
	+ hypothalamus	41,8 %
	+ mesencephalon	41,8 %
Occipital brain	+ diencephalon	36 %
	+ hypothalamus	36 %
	+ mesencephalon	30 %
parietal brain	+ diencephalon	12,8 %
	+ hypothalamus	12,8 %
	+ mesencephalon	15,6 %

beginning of the treatment, the more the size of the cranium increases after the implantations.

4. The essential effect is seen after the first implantation; after the second implantation, the indices reach a distribution pattern corresponding to Gauss's bell i. e. they range within the normal tolerance.
5. Gradually the best effects are attained by combinations of 100 mg of an deeper cerebral area (diencephalon, hypothalamus, mesencephalon) with a hemisphere- or cortical preparation (cerebral cortex, cerebral hemisphere); Tab. 27.
6. The biostatistical remarks relate only to anthropometric measures, which show no strict correlation with the function of the brain i. e. mental efficiency.

Efficiency of the therapy

Assessing and proving the success and shortcomings of a therapy require special factors if a clinical aspect with more than 200 possible individual symptoms is in question. Among them are:

a) a great number of observations;
b) a steady observation over several years;
c) differentiated, provable criteria (parameters).

The first two conditions are fulfilled by treatments of 1780 mongoloid children over 1–25 years. Criteria for assessments were there by hundreds and thousands but could not be evaluated until the «spontaneous development» of untreated mongoloids had been cleared biostatistically. Most of the supporting data had to be established because the medical science had until then been satisfied with global, non-founded, data in this field.

Tab. 28: **Average ages of mothers and fathers of mong. children by the years of the age classes of the children**

Age class	Number of cases	Average ages of mothers	fathers
1953–1961	30	35,0	36,6
1962–1965	54	33,85	35,9
1966	32	32,9	34,0
1967	29	33,5	36,0
1968	54	32,8	34,5
1969	71	33,5	35,5
1970	67	34,2	36,7
1971	61	33,5	36,5
1972	70	32,6	35,3
1973	70	33,7	36,8
1974	51	33,7	36,5
1975	29	31,9	33,9
1979	56	32,1	
1980	64	28,3	
1981	47	30,9	35,1
total	785		

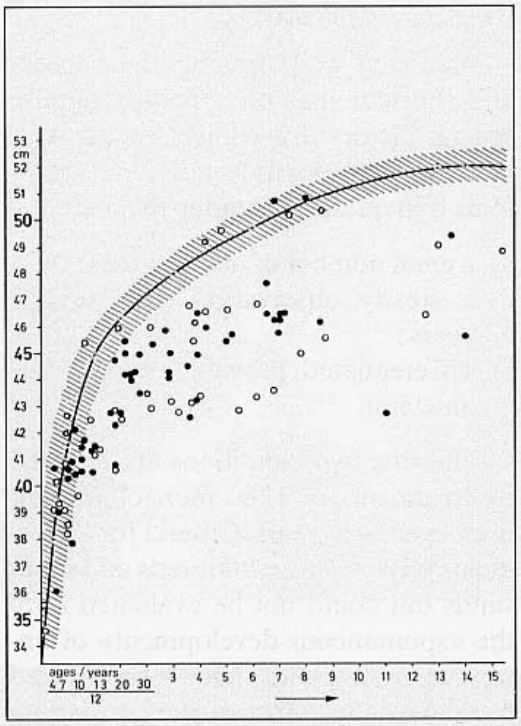


Fig. 238:
Three-dimensional brain-skull quotient

in medically untreated Downs-children:
(n = 100 mongoloids;
● = boys
○ = girls)

Most measurements are clearly below to normal variations.

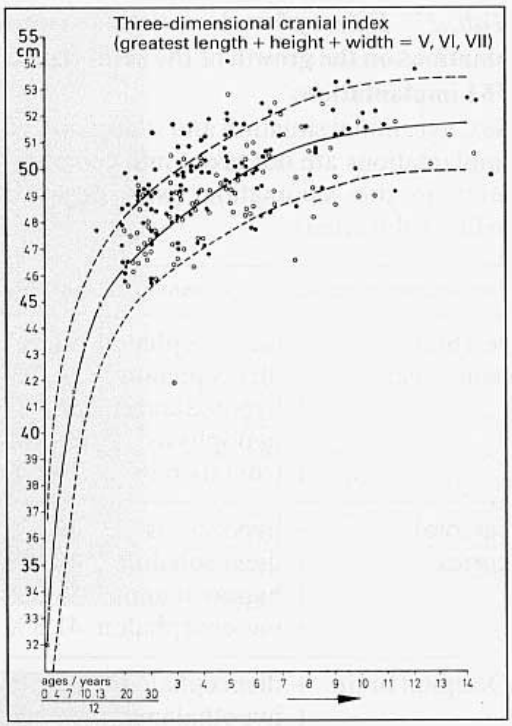


Fig. 239:
Three-dimensional brain-skull quotient

Three-dimensional cranial index (greatest length + height + width = V, VI, VII)

(n = 200 mongoloids, including the 100 cases of fig. 238
● = boys
○ = girls)

After the second inj. implantation of fet. cerebral tissue, the brain-skull-index is mostly normal.

The efficiency of the therapeutic measures was largely proved to a degree seldom possible in medical treatment. The most important results have been outlined hereafter:

1. Stature

Untreated mongoloids are of short to dwarfed stature, boys averaging 148 cm, girls 142. However, it must be stated that also untreated children show considerable variations (plus/minus).

Conclusive information about the influence of the treatment on the stature was not possible prior to an observation period of 6 years and compiling some 1500 values measured. This surveyable space of time shows clearly that the treatment influences the stature without using growth hormones. As in the case of other anthropometric values, the effect differs according to sex. Long treated males reach a final stature of some 161 cm (fig. 234), females 146 cm (1975 study; 1981: 151 cm). The influence of the treatment has been demonstrated for both sexes, especially so by the T-test comparing the ages, and was up to 1976 slighter in girls than in boys.

The measured values remain constant

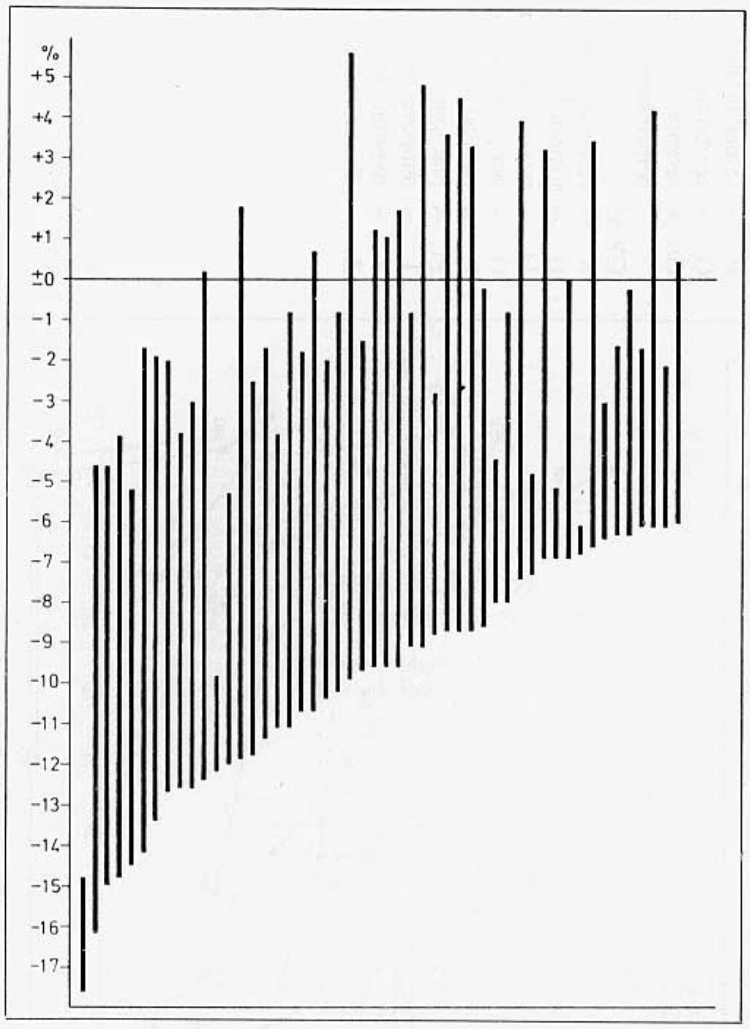


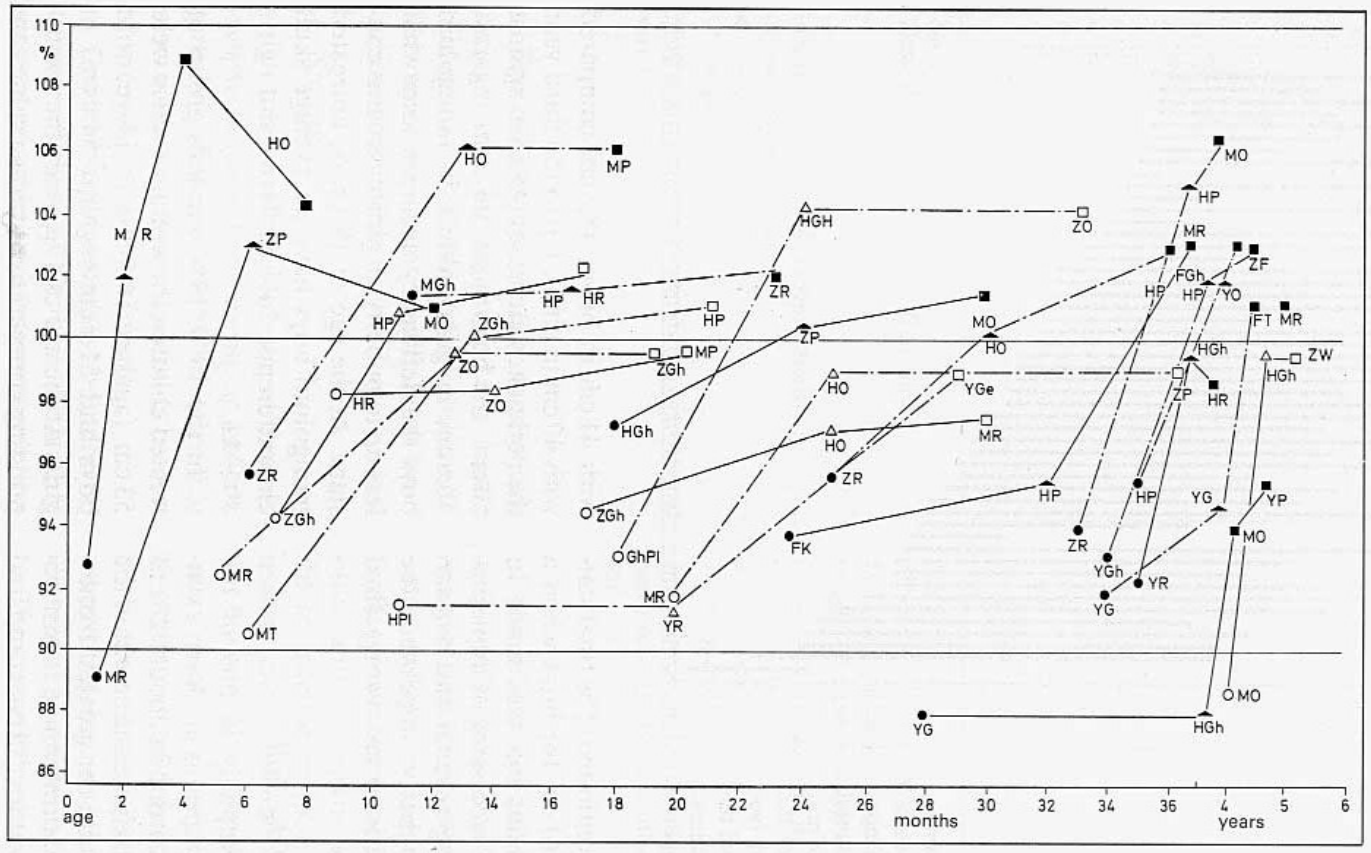
Fig. 240:
Increase of 3-dimensional skull-index in extremely microcephalic mongoloid children (initial values below −6% of normal; n = 50) after the first implantation of lyophilised fetal cerebral tissues. Chiefly considerably increased volumes.

if the therapy is continued. The final stature was about 161 cm for boys when a prospective examination was made in 1979. A changed succession of implantations by including adrenal and ovarian tissues in prepuberty improved the growth of the girls to an average final stature of 151 cm.

Circumference of the skull

Brachy-microcephaly is one of the most constant symptoms of Down's syndrome and is recorded in about 92% of all cases. At the first measurement in the first trimester of life the greatest fronto-occipital skull circumference is just below the normal values (39 cm compared with 41 cm in boys; 38,5 cm compared with 40 cm in girls). Up to the third year the deficiency increases (46.6 cm against 50 cm in boys and 46.2 cm against 48.6 cm in girls). While in mongoloid boys the deficiency becomes somewhat less up to puberty, in girls it remains constant. At the age of 18 years, untreated mongoloid boys have an average skull circumference of 52.7 cm and girls 50.9 cm.

In the 1979/1980 random group of treated children the average values were 53 cm (against 54.5 cm) in 14-year-old boys and 51.8 cm (against 54.0 cm) in girls. At the age of $17\frac{3}{12}$ years the corresponding comparative average values are



F = frontal brain;
G = cerebrum;
Gh = cerebral hemisphere;
GR or
R = cerebral cortex;
H = hypothalamus;
M = mesencephalon;
O = occipital brain;
P = parietal brain;
PL = placenta;
T = temporal brain;
Y = hypophysis;
Z = diencephalon.

Fig. 241:
Individual courses of the three-dimensional skull-index in 20 mongoloid children (● = boys, ○ = girls). Taking the average age as 100 % mean value, the curves show the specific response of the skull growth to the various combinations of implants.
Circle = first implantation, triangle = second implantation, square = third implantation.

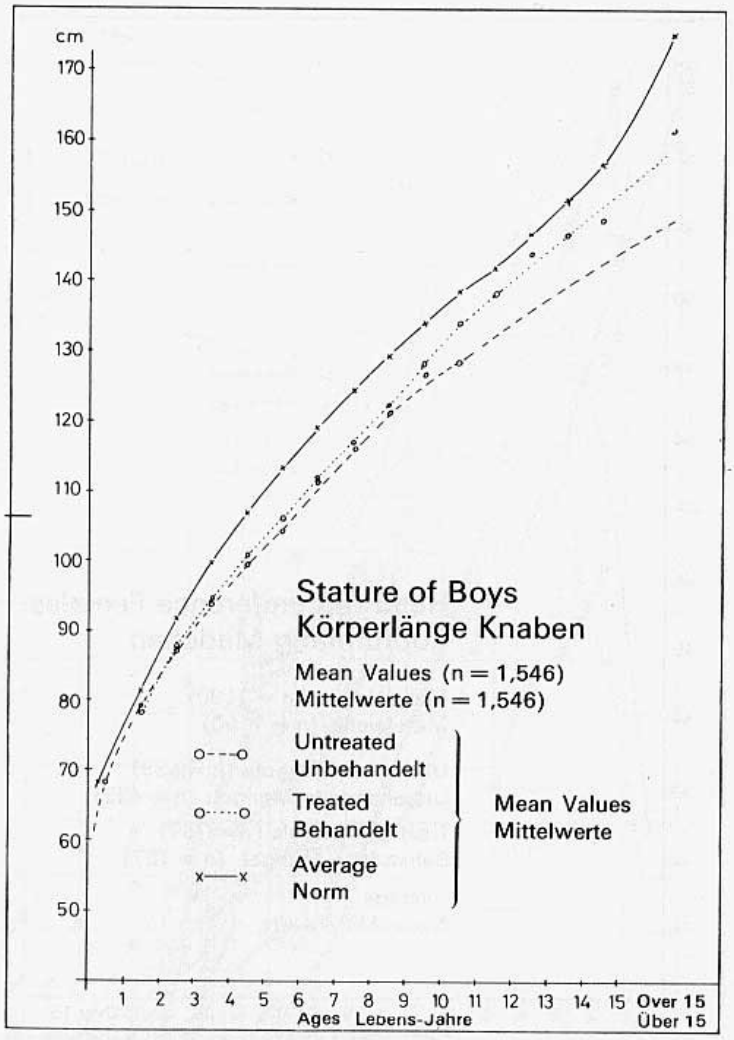


Fig. 242:
Average statures
Boys (n = 1546). The group of treated mongoloids (n = 981) is just slightly superior up to the 10th year to the group of untreated children (n = 565). For the untreated, a final tallness between 148–150 cm may be anticipated, the averages of the treated are about 161 cm and, therefore, in the middle between the untreated and the average of healthy boys (174).

53.4 cm (54.9 cm) in boys and 52 cm (54.4 cm) in girls. The skull circumference of boys reaches 97.3 % and that of girls 95.4 % of that of healthy comparative groups.

To improve the circumference of the head still more, a more specific (with medicaments or implantations) effect on the growth of the cartilaginous preformed base of the skull is necessary. Cartilage, osteoblasts and life as lyophilisates or hydrolysates should be used in the first three years of life (fig. 243).

3. *Brain-volume index*

Whereas the brain-size of untreated mongoloids retards gradually behind the normal average in the course of growth (with the main deficit evolving in the first three years of age), a treatment initiated in early infancy will normalize the index values much or completely. This follows from three-dimensional index measurements on radiographs. This effect can be achieved only with implantations by injections of fetal brain-tissue; an approximation of the skull-size index to the normal average is reached usually after 2–3 implantations (Tab. 27) (fig. 235, 237, 240, 241).

4. *Analysis of development*

In the course of a programmed analysis, the therapeutic effect on the motoric

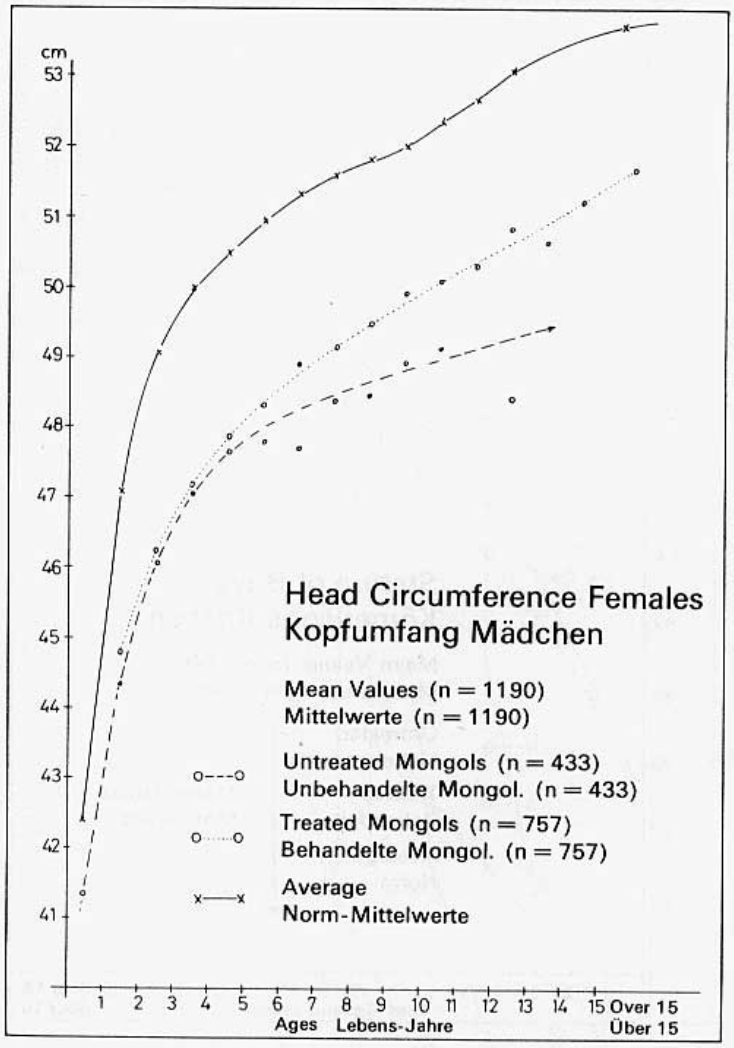


Fig. 243:
Averaged head circumferences Girls (n = 1190). The treated mongoloids (n = 757) show from the fifth year a slight plus over the untreated girls. This difference increases with the growing age; the considerable variations of the mean values among the untreated. At the end of the body growth, the mean head circumferences of untreated mongoloid girls are about 49.5 cm, and 51.5 cm in treated mongoloid girls as against 54.5 cm in healthy girls.

development, fine motoric and coordination, speech, social behaviour and mental development was studied in more than 4000 findings. Whereas untreated children reach usually a state of development corresponding to that of a 4–6 year-old patient, the results achieved by the treatment came up to the criteria of 8–12-year-old children. This creates important conditions for social integration and for learning the elementary cultivation of mind.

5. *Intelligence quotient*

The retardation of mongoloid children affects above all their instellectual capacity. The findings on the intelligence quotient outside the author's clinic showed a considerably higher average of the intelligence age of treated mongoloid children. The intelligence quotient found in infants range from 60–90, and an average increase of the intelligence quotient by 20 points effected by treatment can be ascertained at all ages.

6. *Cultivation of the mind*

Whereas formerly mongoloid children were considered listless and non-educable, and educational efforts centred on practical training, it has become increasingly obvious that treatment can certainly make the majority of these children learn to read, to write and to speak.

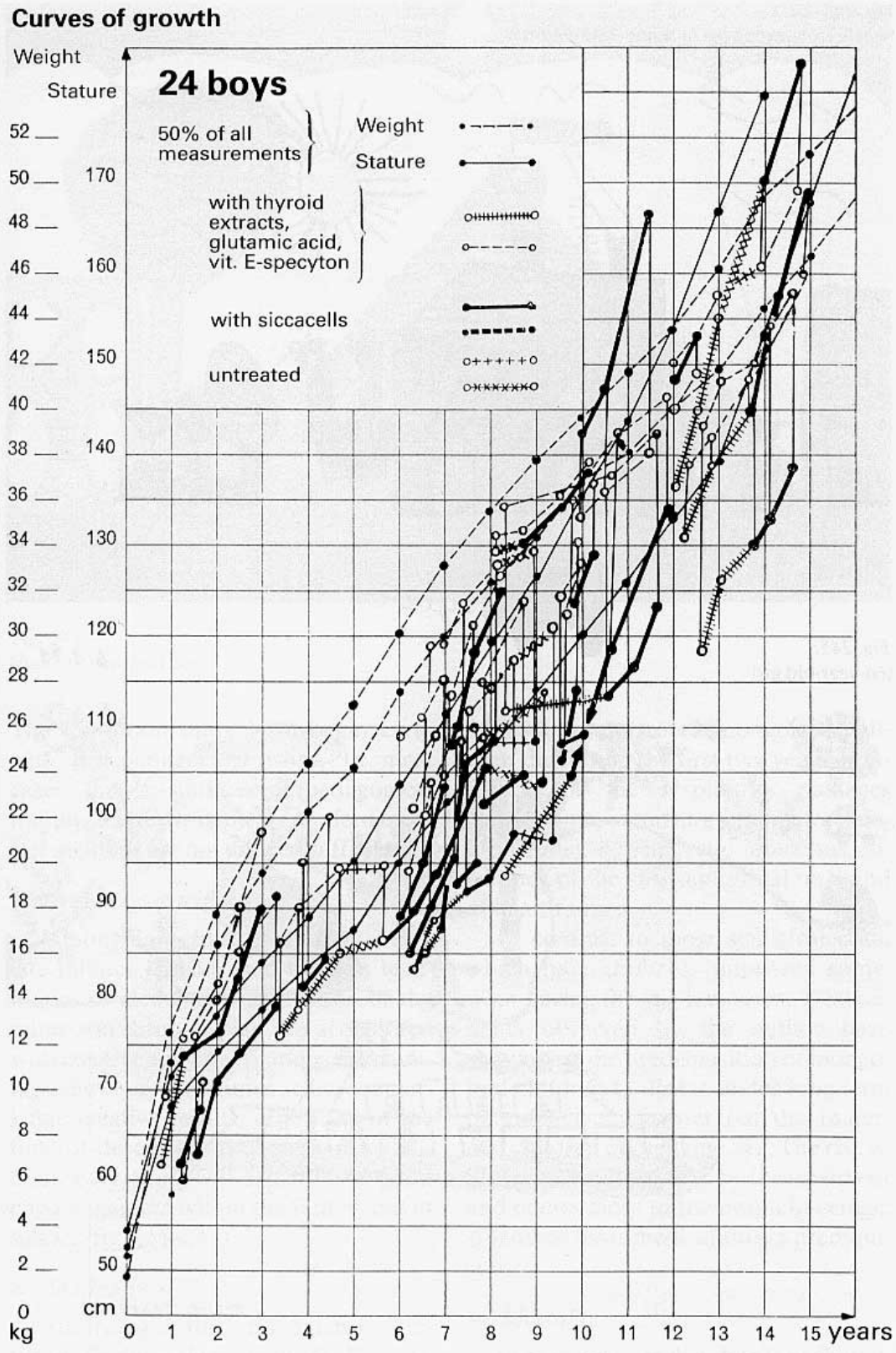


Fig. 244: Courses of the growth of statures in 24 mongoloid boys treated by various methods (H. S. FELDMANN, 1979).

Fig. 245–247:
Scenic representations by mongoloid children

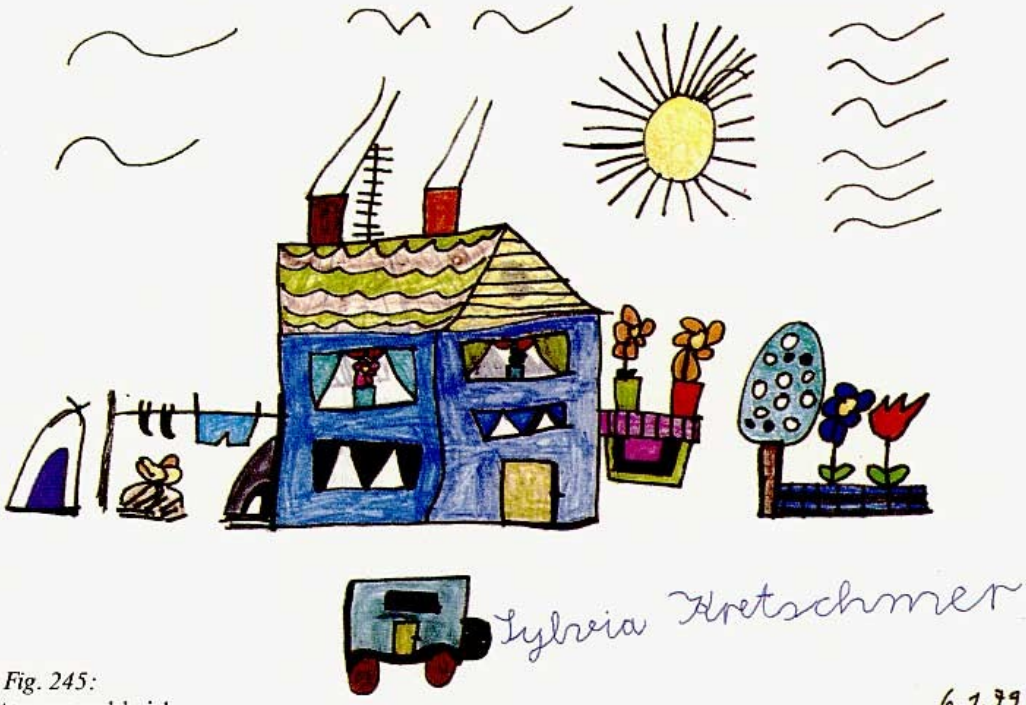


Fig. 245:
ten-year-old girl

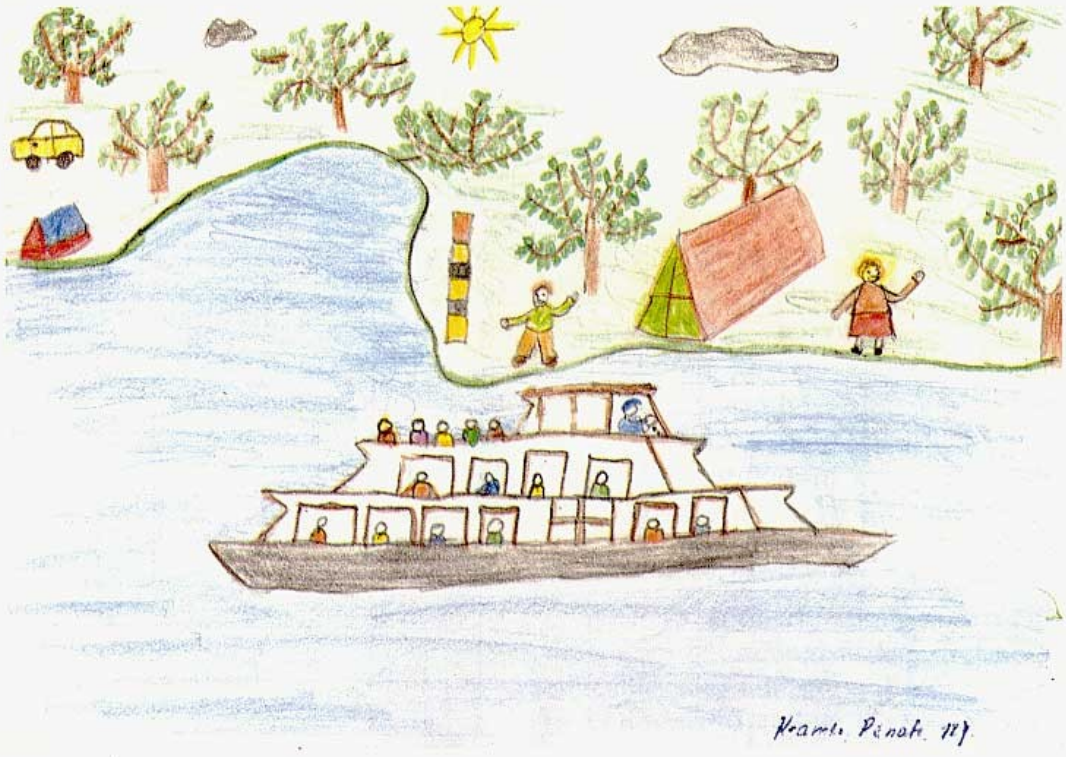


Fig. 246:
twelve-year-old girl

Fig. 247:
fourteen-year-old boy

The important thing is to begin early with the pedagogical work. In most cases, the possibilities of pedagogical training made available by modern medical methods are not utilized sufficiently.

7. Creative capacities

If mongoloid children are early, i. e. in late infancy, encouraged to learn techniques of elementary cultivation of the mind and through play are acquainted with creative activities (handwork, painting), they may sometimes achieve remarkable creative results, especially in the field of descriptive drawing and handicraft. Everything will depend on a good encouragement within the family and at school (fig. 244–247).

8. Morbidity

According to the latest extensive statistical findings (OSTER, 1953); RECORD and SMITH, 1955; CARTER, 1958), 50–60% of untreated mongoloid children die during the first five years of infection of the respiratory passages (pneumonia, stenosing laryngotracheobronchitis), hyperpyretic infections, infections of the gastrointestinal tract and of heart-failure.

In contrast to these statistical data, which have probably improved somewhat during the last few years, 1780 patients observed by the author have shown that the predisposition of mongoloid children to illness under long-term treatment is not greater than that in normal children of the same age. The risk of illness is much reduced by the treatment and comes close to the normal average. Adequate basic medication is a prerequisite.

9. Mortality

In contrast to earlier data (see above), the mortality of the mongoloid children

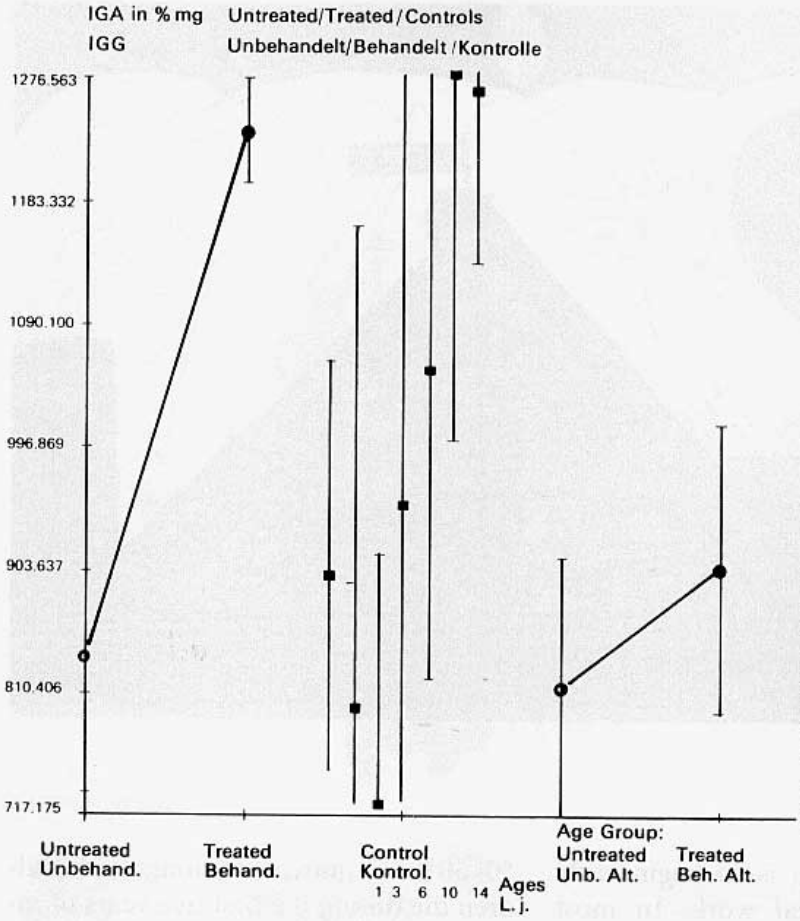


Fig. 248:
The immunoglobulin A is clearly lowered in the mongolian syndrome. The treatment brings the average near to the normal average (central columns). The effect appears smaller when ages are compared (right).

and youngsters is below 3 per cent among the author's patients. The latest statistics established between 1950 and 1960 confirmed for mongoloids a death rate exceeding about 20times that of the normal average. The reduction of the death rate of children to the level of the normal population may be looked upon as one of the greatest results of the long-term treatment. The rest of the deaths within the first ten years of age were chiefly caused by congenital heart-failure serious enough to influence the children's fate alone. The second important cause of death among the treated cases was traffic accidents.

Life expectancy of mongoloid children cannot yet be indicated definitely because this would require observations of at least 2–3 decades. The long-term treatments conducted so far cover 1–20 years. Life expectancy of mongoloid children is nearly the same compared with the age-groups of a «normal» population.

10. Immunological functions

The shift within the pattern of immunoglobulins helps much to reduce the resistance to infection in untreated mongoloid children. Whilst the recurrent infections usually augment the immunoglobulins G, there is a lack of immunoglobulins A and M. Comparative studies on 142 cases showed that the treatment brings the deficient immunoglobulins clearly to a point approximating the normal average (fig. 248, 249) though that average is not attained. Moreover, the resistance to infection is improved. Only children which already suffered from

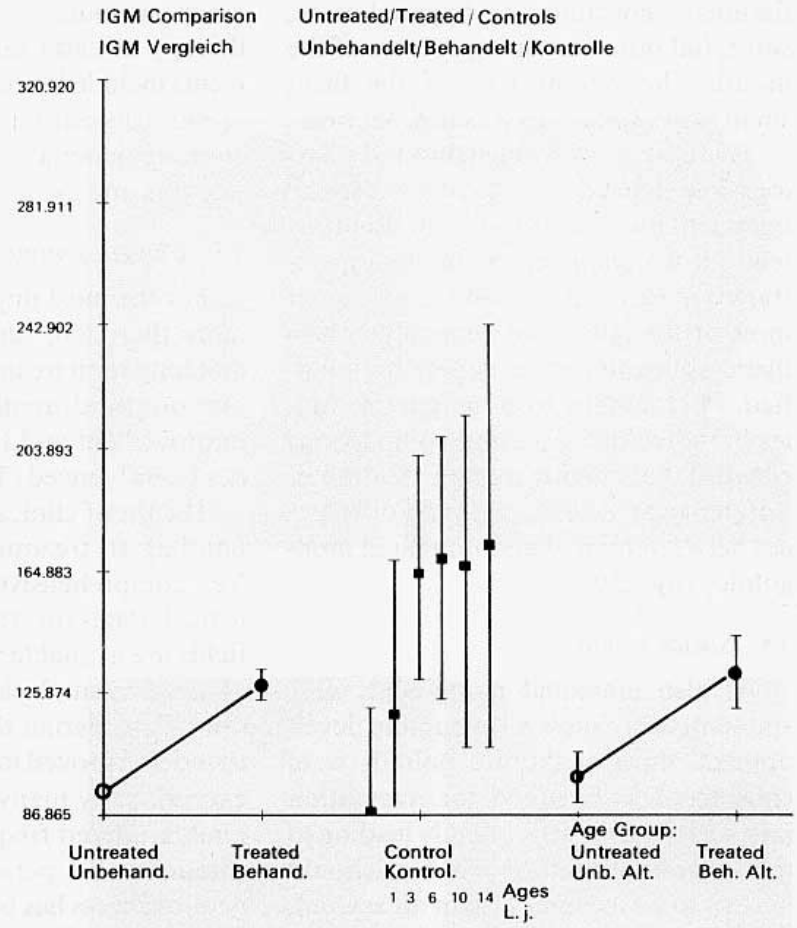


Fig. 249: Immunoglobulins M. Both a general comparison between untreated and treated mongoloid children (left) and a comparison within the age groups (right) show clearly an effect on the immunoglobulins approaching the normal averages without reaching them. The central columns show the normal averages in the various ages (treatments beginning with 142 mongoloid children, 120 healthy children).

chronic infections in the upper respiratory tract (sinusitis, chronic rhinitis, adenoids) before the treatment will react less favourably for a short while.

11. Biochemical parameters

Of the biochemical changes occurring with the mongolism syndrome, the following are of major consequence for retardation:

low serotonin level;
disturbed tryptophane metabolism;
disturbed metabolisms of the vitamins B1, B2 and B6;
disturbed taurin metabolism;
values of uric acid increasing progressively with age;
increase of certain intracellular enzymes;
reduced serum iron;
elevated transferrin;
reduced zinc;
low extracellular calcium levels caused by early calcinosis; comparatively high intracellular aluminium levels, low levels of potassium, manganese and selenium.

It is not yet possible to describe definitely the effect of general treatment on the biochemical aberrations; whilst certain factors (e. g. iron vitamin B2, vitamin B6, uric acid) may well be influenced, the therapeutic concept has still not yet been elaborated to obtain regular patterns. Specially in this field, the therapeutic goals are still too new.

12. Physiognomy

The facies of an untreated mongoloid is characterized by the distorted proportions of the head and the resulting changed physiognomy: slanting palpebral

fissures; epicanthus; hypertelorism; short, flat nose; drooping corners of the mouth; flat middle part of the face; small skull, flat occiput; short, fat neck.

The chance of influencing the physiognomy depends on the time when the treatment is initiated and on how consistently it is conducted. If the therapy is started in early infancy and at the age of three at the latest, the generally unaesthetic appearance can largely be modified. Photographs from long-term studies in individual cases and comparisons between consistently treated children of different age have shown great differences between treated and untreated mongoloids (fig. 250–252).

13. Socialisation

As also untreated mongoloids may spontaneously show a favourable development, most of the mongoloids were considered as unsuited for integration into society, a view frequently leading to the suggestion that the children should be sent to an asylum. Life in an asylum, therefore, was a predestinate fate for untreated mongoloid children.

Treated mongoloid children, particularly those treated at an early age, are definitely enabled to reach a condition assuring their full integration into their families and environment. A poll on the social situation in 220 cases has revealed that the parent – child relation and the children's reaction to their environment are not problematic in most cases.

14. Motor ability

Untreated mongoloid children show a deficient motoric and kinetic ability. The physical appearance is usually limp, with stooping shoulders, dropped lower jaw with mouth open, gawky and straddling gait.

This condition, too, can largely be remedied by treatment, with major importance attributed to systematic physiotherapy in early infancy. The improvements include kinetic reactions, handling of musical instruments (even the piano), working materials and mechanical toys, weaving and gymnastics.

15. Clinical symptoms

For the most important symptoms of more than 200, findings have revealed that long-term treatments can repair well over one third, another third can provide improvement and less than a third cannot be influenced (Tab. 24).

The list of clinical manifestations responding to treatment is not complete. Yet, comprehensive clinical and biostatistical data for the above-mentioned fields are available whereas other fields, as metabolism, lack sufficient investigation. Considering the great numbers of tested and proved measurements and the exceptionally many cases observed, the remark uttered frequently by certain institutions and persons that «no therapeutic success has been demonstrated so far for mongolism» can be denoted only as anachronistic cynism for the parents of retarded children or, possibly as an excuse for own failure.

Development

If in development (= unfolding of the biological powers inherent in the living organism) one sees a complex system of characteristics (present or missing), then it is in principle wrong to try to express this complexity in the abstract figures of an IQ (Intelligence Quotient) or a DQ (Development Quotient). An analysis of development which does justice to the overall biological situation of humans has to consider the following components separately:

a) Coarse motoricity statics
b) Fine motoricity coordination
c) Speech

Fig. 250–252:
Physiognomical changes in the course of an early consistent therapy

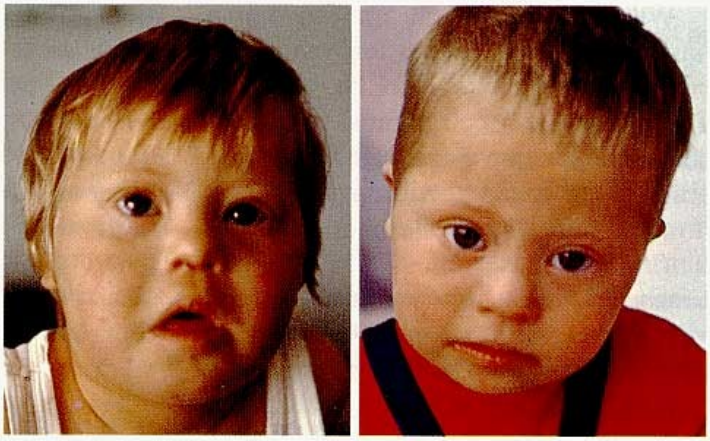


Fig. 250:
Mongol. boy with chronic infections of the upper respiratory passages
a) before treatment
b) 5 months later

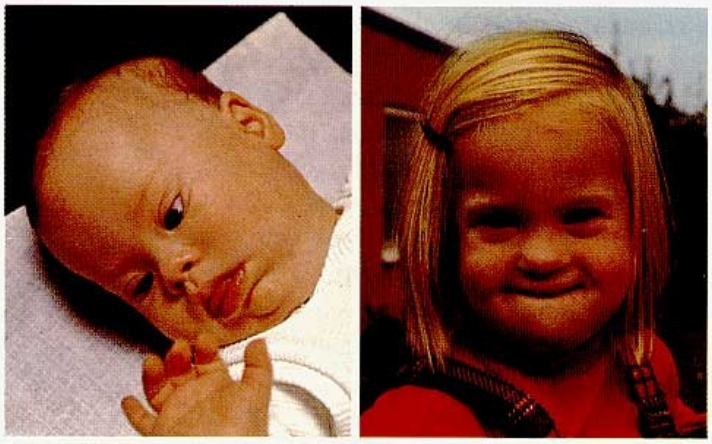


Fig. 251:
Mongol. girl with typical physiognomical changes
a) at the age of 4 months
b) with aesthetical physiognomy after a 5-year treatment

Fig. 252:
Mongol. girl, whose treatment began when she was 7 months old (a), $4\frac{1}{2}$ years later (b).

d) Social development
e) Intellectual development

With a development analysis which has been in use for over ten years, 200 criteria (parameters) can be checked. The individual function must be easy to check and the questions must be answerable by the parents, without any question of doubt. The development tempo is symbolized in a pseudologarithmic, vertically oriented system. At the annual follow-up examinations it does not matter when a function was learned, but rather whether it is (or was) mastered or not. In this way one gains a comprehensive visual overview of the capacities and the failures, the latter at the same time indicating an immediate need for treatment. This analysis is in direct contrast to an IQ

Longitudinal course development.

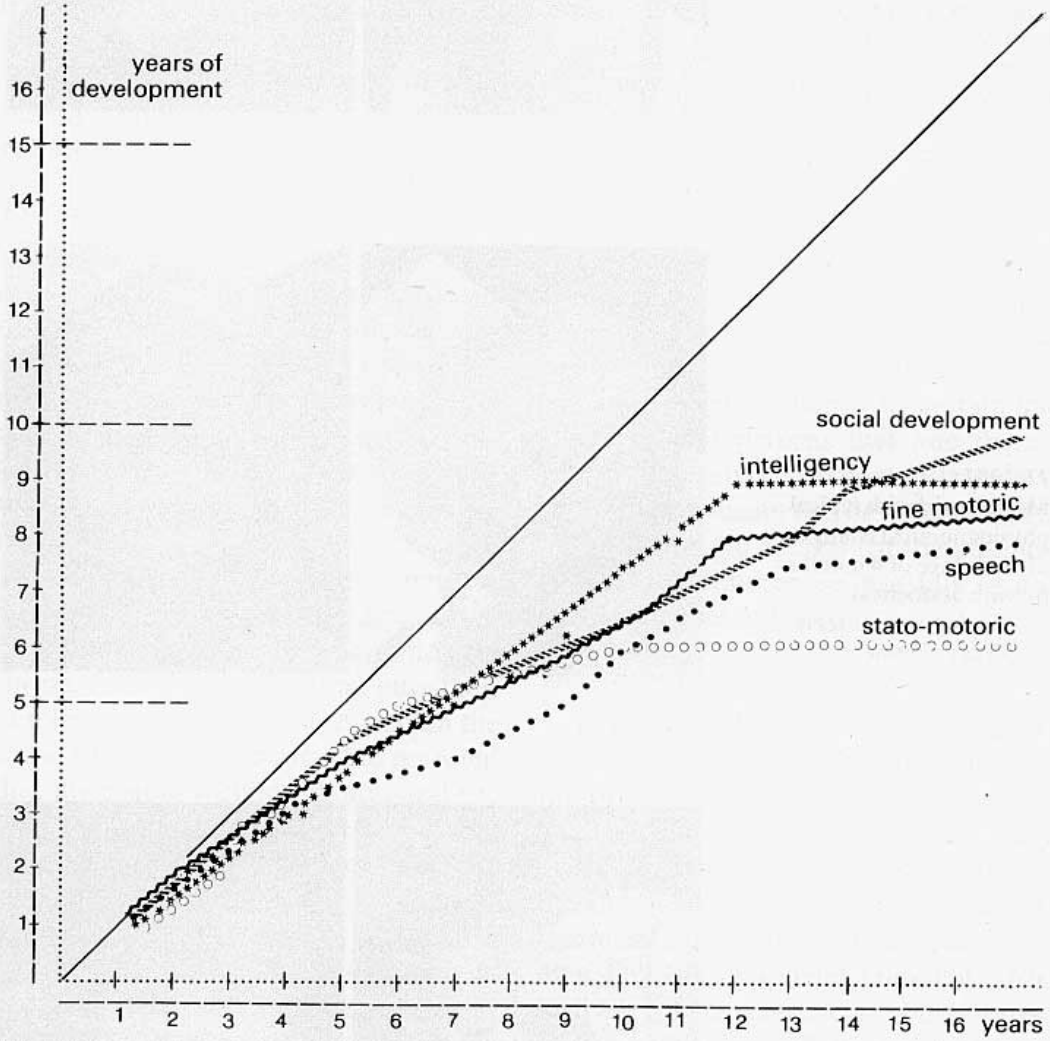


Fig. 253:
Longitudinal course of development in 374 children with Down's syndrome from a prospective investigation carried out in 1980. While in infancy the development almost corresponds to that is retarded. The highest average values which are children with Down's syndrome, of school age, of the average normal child, the development of reached are in intellectual development and social development, which at the age of 14 years correspond to those of normal children aged $9\frac{1}{2}$ years and $10\frac{1}{2}$ years, respectively (for details, see text).

test, which only results in classification into a particular category and has certain advantages but only for official purposes.

If one today (1981) analyses a random sample of children with Down's syndrome who have been treated with drugs on a relatively uniform basis, but whose education and social care has been very different, the development status is as set out below. «Random sample» means children and adolescents with Down's syndrome, with and without other anomalies (e.g. heart defects, gastrointestinal abnormalities etc.), studied over a prospectively defined period. This analysis gives the following average state of development in 14-year-old children with Down's syndrome (Fig. 253):

a) Coarse motoricity statics: average equivalent age 7 years
b) Fine motoricity coordination: average equivalent age 8 years
c) Speech: average equivalent age 9 years
d) Social development: average equivalent age $10\frac{1}{2}$ years
e) Intellectual development: average equivalent age $9\frac{1}{2}$ years

These retardation values have a range of variation of $\pm$ 2 years. Surprising at first was the considerable retardation in motoricity. When one takes into account, however, that after early infancy almost nothing is done as far as motor training is concerned, then this result is understandable, but it does demonstrate the need for therapy during a neglected phase of development.

Of far-reaching significance, however, are the average values in speech, social and intellectual development. If for these, which are very important as far as scholastic advancement is concerned, one takes as a basis an average equivalent age of $9\frac{1}{2}$ years (with a maximum of 12 years), then this means that

the school programm of the first three primary-school classes can and must be made available to children with Down's syndrome.

It is a tragedy that in many «special schools» syllabuses are used in the first three years which are at a lower level than that of the last year in the normal kindergarten. At the age of 8 of 9 years a child with Down's syndrome is generally no longer capable of meeting the normal demands of school to the desired extent, if he has not already acquired a consciousness of achievement and learned to concentrate and persevere at the age of 6 and 7 years. The syllabus of the first three primary school classes, taken at a slower pace than normal, covers, to the limited extent to be expected in these children, reading, writing and arithmetic.

This basic schooling, combined with a good social structure and a mostly above average memory capacity, is the prerequisite for taking up an occupation, under guidance and supervision. The «intellectualization» of most forms of occupational training have certainly made it difficult for those with only average gifts to take up most occupations. These training and apprenticeship regulations have made it completely impossible for the handicapped to complete an occupational training adapted to their practical abilities. It is laws and regulations which present the greatest obstacles to the advancement of the handicapped in their schooling and their working life. Wherever it has been possible to overcome these obstacles adolescents with Down's syndrome have proved themselves to be conscientious, friendly, polite, clean and in most cases also responsible helpers. Social occupations (e.g.

hospital orderlies or assistants) suit them best.

How has the fate of mongoloids changed?

In contrast to the situation existing between 1866 and 1970 it is today no longer disputed that children with Down's syndrome should be treated, nor do people in fact warn against treating them any longer, but the argument still goes on about how to treat them. While a minority of authors, who seem to be totally uninfluenced by the knowledge of the efforts being made in this field worldwide, still propagate «affection» as their main advice, the principal line of attack today in fact ranges between «cytotherapy» and the other methods of treatment. «Whether» has been replaced by «How?». As a result, the sociological and medical situation of patients with Down's syndrome has changed decisively.

The majority of mongoloid children today attend a normal kindergarten without integration problems. The learning effect of the «normal» environment cannot be estimated too highly. Almost all mongoloid children go to school, 5% to primary and elementary schools, 22% to special schools for learning handicapped children and the remainder to special schools for the mentally handicapped. With a few exceptions, such children born in the last 12 years grow up within their families and are hardly ever felt to be «handicapped» by those around them. Whereas up until a few years ago children with Down's syndrome were still excluded from all social insurance schemes, here too there has been a clear change, although a really satisfactory solution still has to be found.

If all the therapeutic possibilities are used, then the overall biological situation of children with Down's syndrome today approaches more closely the average for the normal population than the previous classification under the designation «mongolism». In contrast to the irresponsible claim that therapeutic successes «have not been proven», extensive comparative studies of many different parameters are now available which provide evidence of the effects of therapy. Table 29 gives an overview of this, which will be discussed in detail in the following chapters.

The argument between the theorists about which method of treatment provides the decisive therapeutic effect is futile, because it is with the wholistic therapy that one strives to promote and develop the personality of the patient – assessments on the value of the individual therapeutic steps are not the important thing.

Table 29: **Comparative investigations between untreated and treated children with Down's syndrome are available in the following parameters:**

1. Height
2. Body weight
3. Circumference of the skull
4. Cranial volume index
5. Physiognomy
6. Motor development
7. Fine motoricity coordination
8. Speech development
9. Social development
10. Intellectual development
11. Morbidity
12. Mortality
13. Immunglobulins
14. Metabolic investigations:
    a) Vitamins B_1, B_2, B_6
    b) Na, Cl, K, Fe, Cu, Mn, Zn, Mg, Ca
    c) Ferroxidase I
    d) Transferrin
15. Scholastic situation
16. Creative capacities

The therapy of Down's syndrome as adopted nowadays is one of the most convincing and satisfactory fields of pediatrics. Development during recent years has shown that improved basic knowledge of the biochemical processes has helped to perfect increasingly the therapeutic concept. This therapy is probably the best possible now available but still far from being optimal. Further developments based on present knowledge may necessarily be anticipated for the next years.

Gonosome aberrations

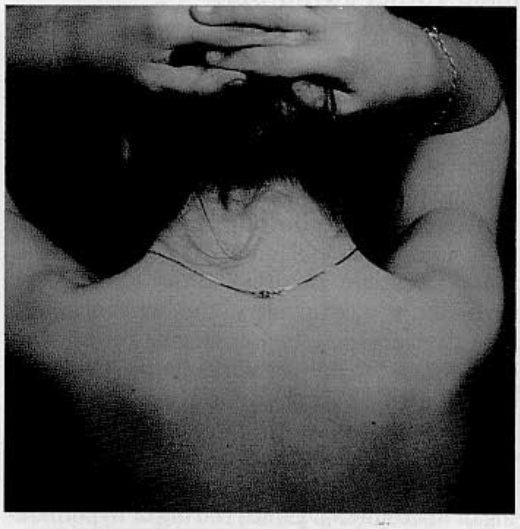
The female determination is localized in the X-chromosome, the male determination in the Y-chromosome. The female sex is homogametic XX, the male is heterogametic XY. There are gonosome aberrations in the structure, in the number and in mosaic combinations.

Turner's syndrome

is the most frequent numeric aberration of the gonosomes. A monosomy X (caryotype: 45, X) is characterized by a number of obligatory and facultative somatic symptoms:

nanism with sexual infantilism; dysgenetic of hypoplastic ovaries;
hypoplasy of the genitals, lack of mammae; primary amenorrhoea;
increased secretion of gonadotropin in the urine.

After the first description by ULLRICH (1930), the aspect has been augmented by multiple facultative abnormalities, referred to as *Ullrich-Turner's syndrome* or as *Status Bonnevie-Ullrich.*



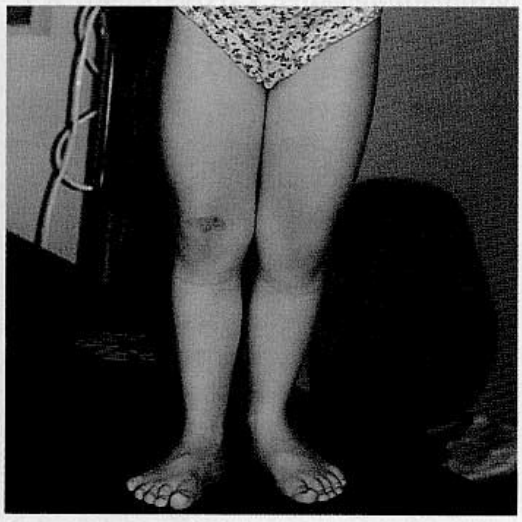


Fig. 254 a, b: Turner's syndrome (45 X)
Carried to term, weighing 2250 g and having a stature of 47 cm when born, nanism ascertained at age of 1 year. (79 cm, −16 cm), 10.3 kg at three years. Typical symptoms: disproportionate nanism, pterygium, small ears, deep limit of hair, shield thorax, atypical finger furrow, male physical appearance (a, b).

To these symptoms belong:
poker face;
deep limit of the cervical hair (fig. 254 a);
pterygium colli;
carp's mouth;

multiple pigmented naevi;
hypoplastic mamillae deficient in pigment,
cubitus valgus;
shortened metacarpal IV;
stenosed aortic isthmus.

Besides these two nosological conditions, there is moreover the *pure gonad dysgenesia (Swyer's syndrome)*, a defective development of the gonads and of the secondary sex characteristics without any further corporal stigmata.

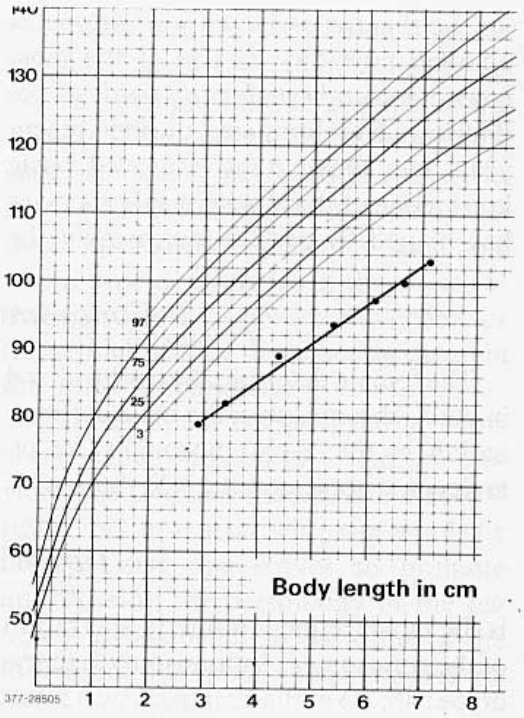


Fig. 254c, Turner's syndrome (45 X)
Regular implantations of adrenal gland, ovary, diencephalon (every dose: 200 mg of lyophilisate) at intervals of 6 months, ovibion, later combined with cortiron, brought the growth rate to about 6 cm per year so that the deficit of stature has not much increased since the treatment began (c).

Male Turner's syndrome

Cytogenetically determined by the chromatin-negative karyotype 46, XY, this aspect is also called *«testicular germinal dysgenesis»*, *«male gonad dysgenesis»* or *«Noonan syndrome»*. The symptoms are the same as those of Turner's syndrome, with infantilism, hypoplasy of the testicles and nanism as the most important. Lymphangiectatic oedemata and skeletal abnormalities especially on the hands (brachycarpy, brachydactylia) are more frequent, pigmented naevi rarer than in female Turner's syndrome. The testicles are hypoplastic, dystoptic and secondarily injured with advancing age. There are less 17-ketosteroids in the urine. The gonadotropin level is low also after puberty (hypoganadotropic hypoganadism). There is no or little secondary hairiness on the body, the development of bone is evidently retarded (fig. 255); adults develop osteoporosis and premature regression (HIENZ). X-monosomy has not yet been detected in male Turner's syndrome.

Fig. 255 a, b, c:
Male Turner's syndrome ▶
A boy of 8 years, who moreover suffers from a valvular pulmonary stenosis, is presented for the first time with a nanism of minus 18 cm. Dystrophy, mild ptosis bilaterally, deep ears, shield thorax; breeches-like thighs, the testicles are small and soft, palpable in the inguinal canal. An extremely loud, high-frequent, long-drawn-out noise due to the valvular pulmonary stenosis can be heard. The ossification at this time corresponds to that of a $4\frac{1}{2}$-year-old boy and thus conforms much to the real stature (a).
Beginning of treatment by implantation of 100 mg of male adrenal gland, 100 mg of hypothalamus and 120 mg of testis.
Basic treatment: cortiron and primogonyl.
With implantations at half-year intervals, the boy grows 14.5 cm within $2\frac{1}{2}$ years, shows a growth rate (c) somewhat above average during that time and recovers much of the deficit also with respect to the ossification. The testes have grown, but still palpable in the inguinal canal.

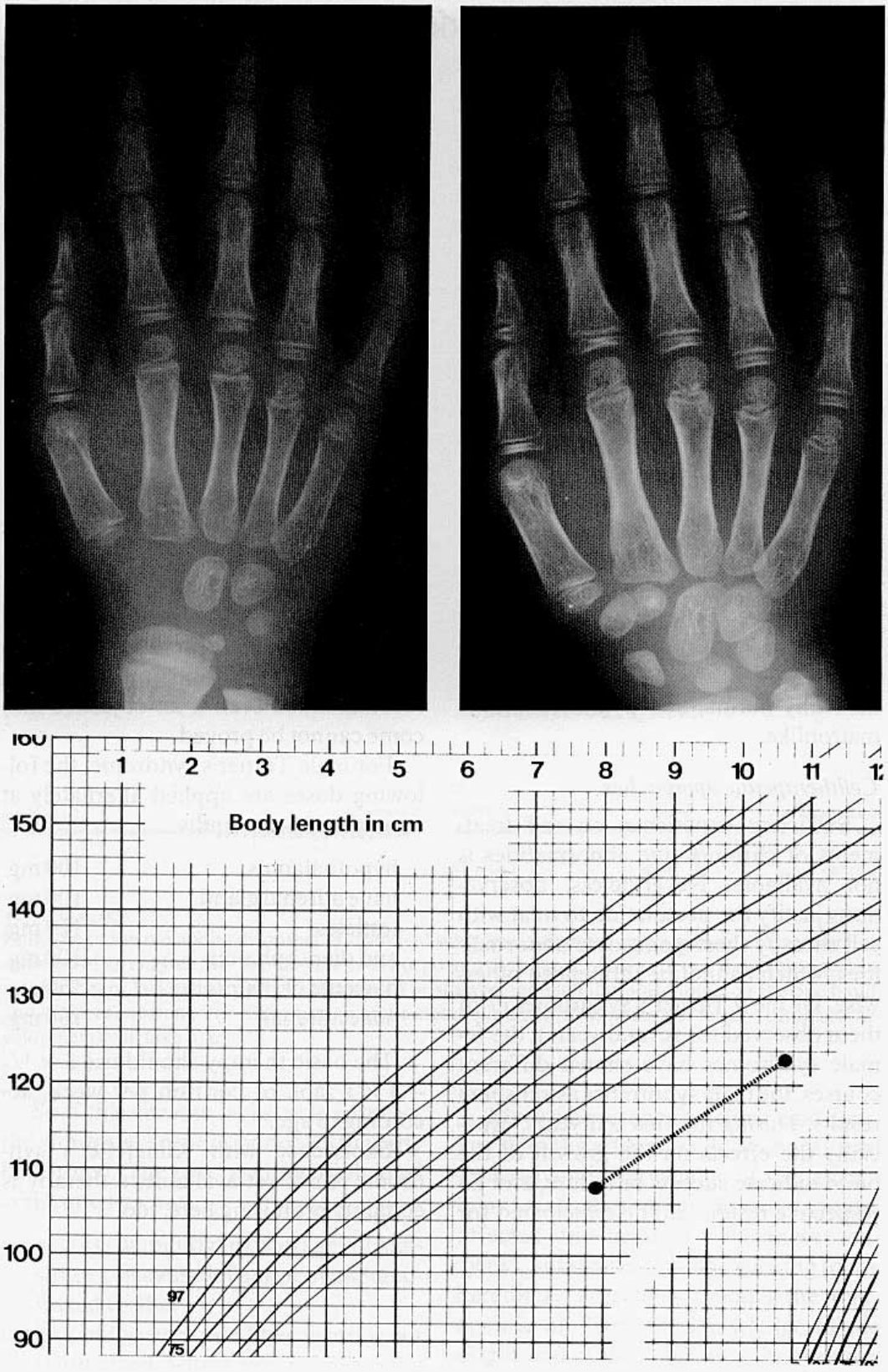

160
150
140
130
120
110
100
90
1
2
3
4
5
6
7
8
9
10
11
Body length in cm
97
75

Fig. 255 a, b, c

is based on the constellation XXY of the sex-chromosomes. As the picture varies much with the central symptoms hypoganadism plus high-growth, Klinefelter's syndrome is referred to as classical (XXY) and atypical; numerical, structural aberrations and sex-chromosome mosaics are found in various constellations. The nucleo-morphological findings are chromatin-positive. The testicles are hypoplastic due to tubular sclerosis and hyperplasy of interstitional cells.

The facultative symptoms comprise:

partial baldness;
scanty or lacking beard,
gynecomastia,
hairiness of female pubes,
osteoporosis.

The structural build includes the following types: eunuchoid, dysplastic, somatically normal and pyknic-feminine-matronlike.

Celltherapeutic approaches

Sufficient experience on cell treatments of chromosome abnormalities is not available. Nevertheless, observations justify the postulation to treat with cell therapy these gonosome abnormalities, which cannot be influenced otherwise. Of the 9 Turner's syndromes (7 of them observed for several years), the female syndromes have shown different courses, the male syndromes astonishing results. During the first ten years, especially the effects on the growth of the build indicate success or failure, and no respective results can be anticipated for the female Turner's syndrome after the 10th year of age.

For the male Turner's syndrome, however, the effects on the growth of the body, the ossification, the social behaviour and the impulse are convincing (fig. 255 a–c); not only the growth rate is normalized but also the lacking ossification is largely completed (fig. 255 b, c).

For female Turner's syndrome,

female adrenal gland	100 mg
ovary	120 mg
hypothalamus	100 mg
alternating with:	
placenta	150 mg
ovary	120 mg
female adrenal gland	100 mg

are used at intervals of 5–6 months.

A substitutive basic therapy with 2–3 × ½ tabl. of cortiron per week and ovibion dosed according to age daily is recommended even if an objective outcome cannot be proved.

For male Turner's syndrome, the following doses are applied alternately at intervals of 5–6 months:

hypothalamus	100 mg
male adrenal gland	100 mg
testicles	120 mg
and diencephalon	100 mg
placenta of male fetus	150 mg
male adrenal	100 mg.

The basic therapy should use 3 × ½ – 3 × 1 tabl. of cortiron per week, according to age.

Experience with Klinefelter's syndrome is not yet available, a therapy is certainly promising here, too.