Experimental fundaments

Apparent progress is the subject of discussions, real progress must be obtained by fighting. This millenial law of science must be stated first if cell therapy is to be understood in the system of modern medicine. A therapy originating from empiricism that claims the capability of regenerating effectively biological structures and of thus influencing ailments defined as uninfluenceable by the modern dogma of medicine, must achieve and prove more than an ordinary chemical substance. Same as in Galilei's times, dogmatists refuse to see what is obvious: medicine is about to cross the threshold between the chemical age and the biological epoch, which depends on the principles of the living substance – and does not rely on the usability of accidental chemical products for the organism. This step from an apparently solid building, often referred to as dogma, is a challenge and arouses hope. Challenged are persons and institutions who identify medicine as a natural science with chemistry and classical physics and, consequently, misunderstand the complexity of life and of its spiritual content. Hopes for the people who «according to the present state of medical knowledge», as the arrogant saying goes, cannot be helped. The fight of dogmatists and institutions aims at the legendary fame of a therapy that helps primarily and for its success was secondarily compelled to furnish proof.

Definition

The name «Cell therapy (originally: cellular therapy)» was derived from the cellular pathology (VIRCHOW). In its most neutral version it means the use of cellular material for therapeutic purposes. In this form, cell therapy belongs to the oldest medical treatments, and includes the following methods:

Transplantations of bone-marrow;
Blood-transfusions;
Implantations of thymus;
Transfusions of thrombocytes;
Concentrates of erythrocytes;
Suspensions of leukocytes.
Transplantation of
- fetal liver cells
- fetal spleen cells
- fetal bone-marrow
- pancreatic cells.

In colloquial usage of the last years, the concept of cell therapy has been identified more with the use of fetal xenogenic tissue. In this restricted formulation, the method can be defined as follows:

Cell therapy is an implantation by injection of (xenogenic) fetal or juvenile suspensions of cells or tissue in physiological solution. The implantation provides the organism of the recipient with a great number of biochemically demonstrable substrates and enzymes found in this concentration and composition only in juvenile tissue.

Tab. 4: **Cytochemical identification of enzymes and substrates in fetal tissues**

Enzymes	Substrates
lactatedehydrogenase	desoxyribonucleic acid
non-specific esterases	(FEULGEN; methyl-green pyronin)
alkaline phosphatase	ribonucleic acid (methyl-green pyronin)
dopa-oxydase	nucleotides (toluidin)
adenosin-triphosphatase (ATPase)	alpha-amino groups (ninhydrin)
	SH-groups (after FREDERICH)
	acid and basic substances
	(haematoxylin-eosin; ferric
	haematoxylin)
	lipoids (sudanoblack B)
	lipoid-nuclear coloration (scarlet)
	glycogen (BEST-carmine; PAS; PAS
	after ptyalin)
	polysaccharides

The implantation by injection has essential advantages over the conventional procedures of implantation; they can be outlined as follows:

1. *Implantations by injection bring about a rapid dispersion of the implanted cell material all over the body.*
2. *There are no injuries by implants owing to deficient blood supply during the disintegration of the implant.*
3. *Thanks to the form of suspension, a rapid infiltration into the metabolic processes is possible.*
4. *Organs inaccessible (brain, endocrine glands) or difficult to attain (kidney, liver) by contact transplantation can be reached.*
5. *The fetal tissues with their higher biological potencies are conveyed in the recipient on his own ways of metabolism and used at structurally suited sites. So the organism itself controls and effects a selective incorporation.*

For the implantation by injection, the *intravenous, intraperitoneal, intramuscular* and *subcutaneous* ways of application, theoretically, come into question. The most physiological way, probably, is the intraperitoneal application, which, however, should be used like the intravenous application in exceptional cases only to avoid the risks connected therewith. Most of all, the intramuscular application has been used so far; it constitutes a middle course between the subcutaneous and intraperitoneal ways; its disadvantage: the intramuscular application provokes stretchings and hemorrhages at the sites of injection, which cause secondary processes. The method of choice is the deep subcutaneous, epifascial dispersion of the implantation depot. The injection should be effected completely atraumatically i.e. without resistance, even if large volumes are in question. The injections should preferably be applied to the outer quadrant of the gluteal area and the skin of the abdomen.

Fig. 48–108:
Biochemical substances (substrates and enzymes) contained in lyophilised fetal tissues.

Fig. 48:
Thymus belongs to the tissues *rich in DNA*. Methyl-green (= DNA)-pyronin (= RNA) staining.

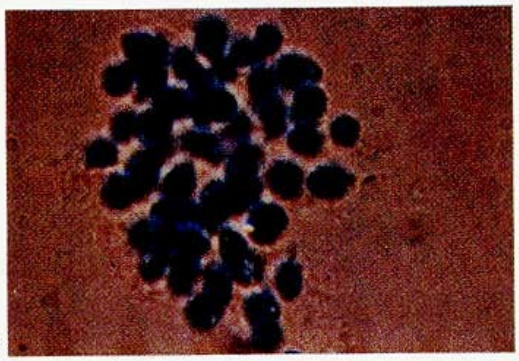
Fig. 50:
Identification of *alpha-amino-acid* with ninhydrin.

Fig. 52:
Nucleotides in freshly taken thymus tissue.

Fig. 49:
Fetal cartilage is *abundant in DNA and RNA* (red). Methyl-green-pyronin staining.

Fig. 51:
Identification of *dopa-oxydase*. Laidlaw-Blackberg solution. Concentration of enzymes in the *brain.*

Fig. 53:
Nucleotides in lyophilised thymus tissue. The comparison between fig. 52 and 53 shows in the lyophilisate a higher concentration of substance in proportion to the volume.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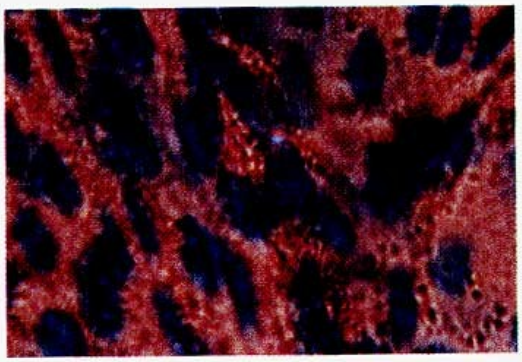
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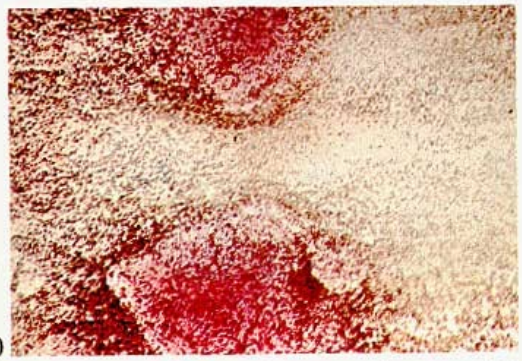
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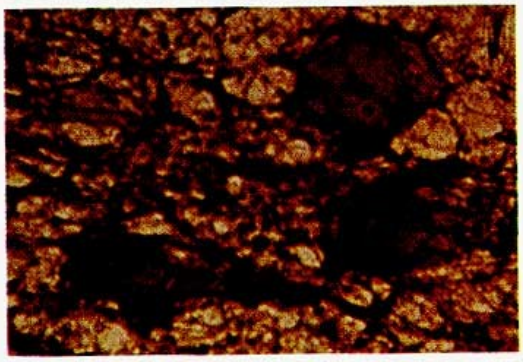
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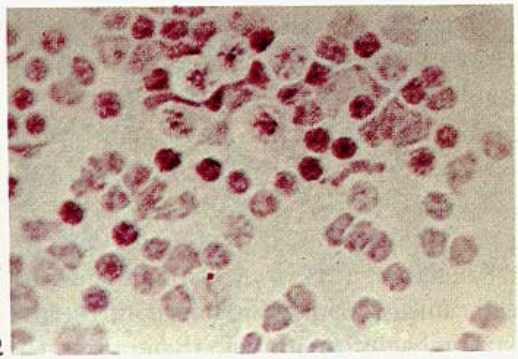
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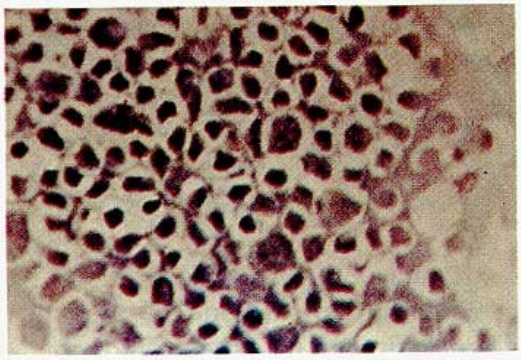
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Fig. 54:
Fetal kidney, panchromatic after PAPPENHEIM: tubular formation.

Fig. 55:
Fetal kidney. Hematoxylin-eosin colouration. Acid and basic substances.

Fig. 56:
Fetal kidney. Toluidin-blue: *nucleotides* in the nuclei.

Fig. 57:
Fetal kidney: Feulgen colouration: *desoxyribonucleic acid* in the nuclei.

Fig. 58:
Fetal kidney: sudanoblack B: whole *lipoids* occurring mostly in the nuclear membranes.

Fig. 59:
Fetal kidney: Best-carmine colouration: only little *glycogen* can be traced in fetal tissues.

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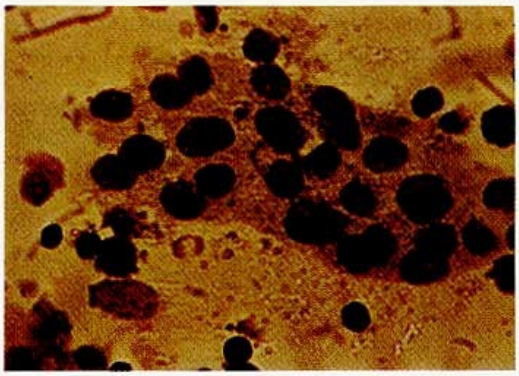

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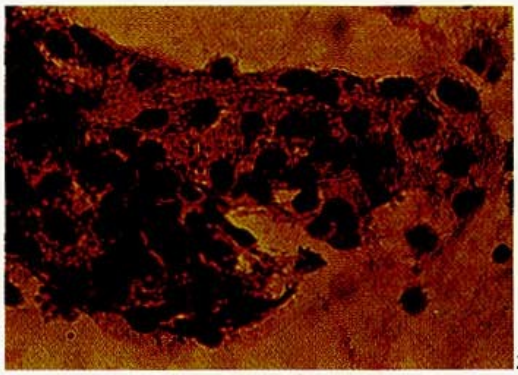

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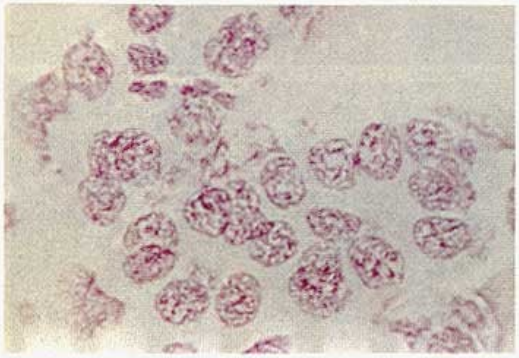

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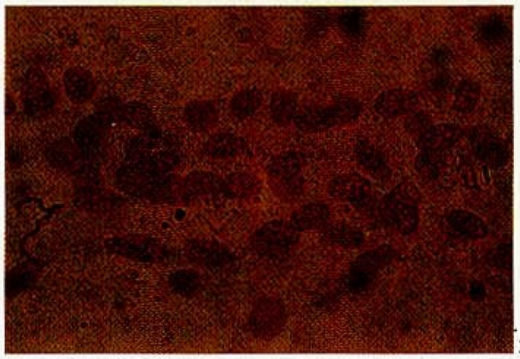

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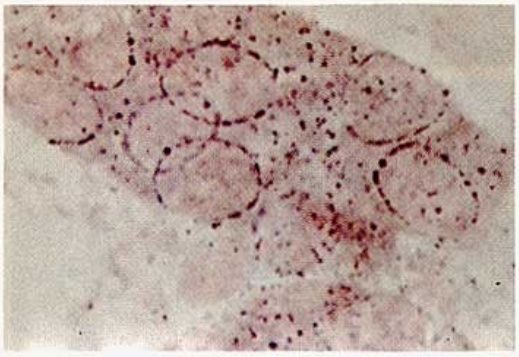

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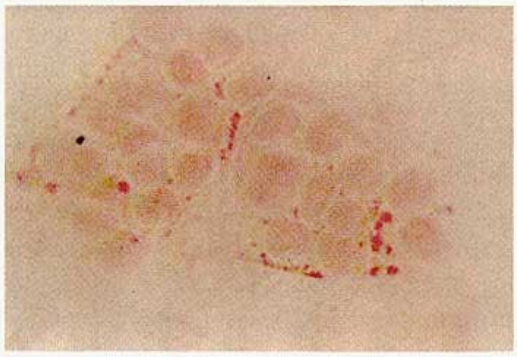

Characteristics

Fetal tissues were chosen first for theoretical considerations, which were later substantiated biochemically and immunologically.

The use of xenogenic (heterologous) suspensions of cells is a necessary consequence of present legislation.

Fetal tissues are used because they contain high concentrations of biochem-

ical substances (substrates and enzymes), concentrations necessary to assure the high demand for material for the growth of fetal structures.

The second reason for the use of fetal cells is the small antigenicity of fetal tissues.

An essential characteristic of cell therapy is the application in the form of implantation by injection. This method is more expedient than the customary procedures of transplantation because the biochemical substrates and enzymes can be used by the body direct, without any secondary degenerative symptoms caused by transplantation changing and rendering them incompatible.

The therapeutic material

The injected suspensions of cells and tissue are taken up by the recipient's organism through phagocytosis and subsequent degradation, and disintegrated into submicroscopic size within two days. The active substance is constituted by the plurality of the ingested biochemical substrates and enzymes. Of the many biochemical substrates thus made available to the recipient's organism, only part of them have been traced so far in the therapeutic materials of the cellular products (see table 4, fig. 49–108).

The «remedy» is reduced tissue, which is injected by doses of 15 to 55 mg/kg of bodyweight = 2–10 mg/kg of bodyweight of lyophilised substance. An injection of 100 mg of lyophilisate contains 45–75 mg of protein, of which 3–8% of the dry weight (= 6–20% of the whole protein) pass into solution after suspension. The fundamental pharmacological studies were conducted by NEUMANN (1961–1963).

Conclusion:

Tests for pyrogen under DAB 6 did not indicate any pyrogens in doses of 100–150 mg/kg of body weight (rabbit).