

NINTH  
INTERNATIONAL  
CANCER  
CONGRESS

October 23 – 29, 1966  
Tokyo

# Experimental Chemotherapy New Antitumor Agents III

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The anticancerous effect  
of macromolecular  
extract from the  
maternal portion of the  
placenta (decidua), (0730)

Separatum

As reported by GRABAR, comparative studies in genetically identical pure animal breeds on the molecular composition of tumour cells, as well as healthy adult and embryonal cells, have revealed that certain substances found in normal cells are absent in cancer cells while, on the other hand, various components of cancer cells are not found in the cells of a healthy adult organism, although some of them have been discovered in embryonal cells. Thus, it follows that in the presence of cancer structural genes, which were active in embryonal cells, are re-activated. Presumably, these are phylogenetically very old genes, or desoxyribonuclein acids, which cause a variety of phenomena including aerobic glycolysis and the loss of contact-inhibitive properties. The re-appearance of embryonal cell substances in cancer cells suggests that as a result of cancerisation chiefly genetic regulating mechanism, such as regulating and operating genes, are injured.

If in accordance with HAECKEL'S fundamental biological law ontogenesis is only a short repetition of phylogenesis, it follows that these phylogenetically old structural genes are already activated in the earliest stage of a new life in the trophoblast or chorion cells. Here, comparisons with tumour cells are possible, since tumours originating from chorion cells belong to the most malignant types of cancer. Apparently, the synthesis chains controlled by these phylogenetically old genes lack type specificity, since they were generated in very early stages of phylogenesis. Lodging of the fertilized ovum in the maternal organism produces a sudden change in the endocrines favouring ergotropic, growth-promoting tendencies, whereby the change originates in the chorion cells. In cancer, a similar reaction is found in the endocrine predisposition to the disease; it is, therefore, highly probable that cancer cells can also cause changes of this nature.

By the maternal organism, the decidua, that is the maternal portion of the placenta, is formed as a defensive wall, which affords protection against cellular attack by embryonal cells, and also against endocrine-vegetative changes. Thus, the functions of the decidua are antagonistic toward the embryonal portion. In my opinion, the active factors are "internal suppressors", which penetrate into the chorion cells, where they inhibit the regulating mechanism of the phylogenetically old genes, as a result of which the autonomic characteristics and the anomalous metabolism are suppressed. Equilibrium of the vegetative reaction in the maternal organism is restored by trophotropic counter-reactions, which originate in the maternal portion of the placenta. As a result thereof, the intensity of biological immunisation processes is also enhanced. During normal gavidity, cellular and functional equilibrium of maternal and embryonal portions of the placenta is established, which, in the event of gestoses, appears to be disturbed in favour of the embryonal portion.

In view of the functional similarity existing between the trophoblast and cancer cells, I decided, in co-operation with TRIEBEL, to use the maternal portion of

the placenta for cancer therapy. In demi-placenta types, the maternal portion can be processed fully independently of the embryonal portion. As a highly preservative method of digestion, I have developed a water-free vacuum-acid fume hydrolysis at normal temperature. As implied by the name, the powdered organic preparation is digested under vacuum and exposed to the action of acid fumes. Thus, water solubility of cell substances is materially improved; the process also ensures a reduction in type specificity and optimum preservation of organic specificity. At present, experimental work is being carried out aiming at the isolation and enrichment of the active factors.

For cancer treatment, the dissolved organic preparation is administered by parenteral injection as isotonic solution with an admixture of  $10^{-6}$  (ten to the minus 6<sup>th</sup>),  $10^{-9}$  and  $10^{-12}$  per ml injection solution. The surface-active ingredient prevents adsorption of molecules at the ampoule wall, improves permeability of bio-catalysts, reduces their antigenic properties and has a preserving effect. Since the concentrations used are below the biological immunisation threshold, continual substitution is possible. Hitherto, experience has indicated that malignant properties of tumours and the endogenous predisposition to cancer are suppressed, provided that treatment is carried out over an extended period.

Also recombination seems to be possible, whereby the genetic defects are permanently remedied. Based on analogous conclusions drawn from experimental work in the field of genetics, however, recombination rate is relatively low, as a result of which this factor appears to be only of minor importance.

From various hospitals, as well as general medical and veterinary practice, favourable results obtained from the above treatment have been reported. WRBA found in tumour explantations an inhibition in metabolism up to as much as 30 per cent, together with a similar increase in hepatic cells as measured by the turnover of radioactive phosphate.

In view of the simultaneous stimulation of metabolism in healthy cells it would appear that the cellular defence mechanism against cancer is improved. JACHERTS, JACHERTS and MAY demonstrated in a cell-free system for albumin synthesis after inactivation that synthesis processes can be restored with the aid of corresponding extracts from the embryonal — not the maternal — portion. Future test work will be devoted to the degeneration of cancerous properties — particularly aerobic glycolysis —, restoration of contact-inhibitive properties, as well as stimulation of vegetative reaction and generation of antibodies.

According to an oral communication Prof. STIEVE of Munich has found with a female patient that a cancer-metastasis remained stationary, or even decreased as a result of treatment with dilute solutions from the maternal part of the placenta. In the ensuing radiation-therapy it was found, that the radiation sensitivity of this metastasis was considerably reduced in comparison with the

parent tumour. This could indicate a decrease in malignity, particularly as the radiation sensibility of a tumour is proportional to its malignity and growth-tendency.

Specific administering of the isolated maternal or embryonal portion of the placenta has no adverse side effects, since bio-catalysts are used, which, however, are generated only during pregnancy by the human organism in corresponding concentrations, although, in principle, these inhibitors of phylogenetically old genes are found in every normal cell.

Thus, this method of cancer treatment may be referred to as "eubiotic regulation therapy".

We could now also consider applying our high-molecular organ-extracts in carcinocolytic cancer-therapy. The cancer-cells will presumably be stimulated by the foetal part of the placenta and thereby made more sensitive to external effects. Extracts from the embryonal portion has no cancerogenous effect. Such a sensitivization could also result from application of surface-active substances, as suggested by me in 1959 for tumour-therapy. Prof. v. ARDENNE intends to try out extracts from the foetal part of the placenta and surface-active substances in his further experiments in connection with syncarcinocolysis in several stages.

In this therapy various substances with cumulative or multiplicative effects are applied simultaneously or successively, in order to kill cancer-cells in combination with extreme whole-body hyperthermy. Every enhancement of the sensivity of cancer-cells in comparison with normal cells improves the prospects for selective killing of the former.

If cancer-cells nevertheless survive they could be limited in their autonomous properties and in their growth by further treatment with the factor from the maternal part of the placenta. This could bridge the time until a second treatment could take place. Immediately before and during the second treatment, the extracts from the foetal part of the placenta could again be applied together with surface-active substances to sensitivize the cancer-cells for the killing-treatment.

A repeated alternation of cytolysis and cytostasis could bring us nearer to an ideal cancer-therapy.

For cancer-prophylaxis, repeated treatment with highmolecular extracts all with the corresponding factor from the maternal part of the placenta could be a suitable method.

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