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CRITICAL SURVEY OF THE STATE OF CANCER RESEARCH WITH SPECIAL REFERENCE TO THE LONG-TERM MEDICAL THERAPY WITH NITRILOSIDES (LAETRILE, VITAMIN B-17)

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ABSTRACT AND COMMENTARY

Cancer is more common in those people suffering from primarily of an immunosuppressive state. The standard highly toxic so-called anti-neoplastics such as endoxan or cyclophosphamine, as well as all other alkylating agents, depress the immune resistance dangerously. On this point Dr. Nieper writes —

> "I do not understand, in principle, why so much work and money have been put into researching alklylating substances, under misleading conditions experimentally testing on rapidly growing grafted tumors, to boot. Commonsense should force one to give up such a program as useless from the very beginning."

The use of analeptics — agents stimulating tissue oxygen uptake — are discussed as means of increasing host metabolic response to cancer. K-Mg-Aspartate is primary among such. Calcium diorotate as well as lithium orotate or citrate are described as germane to fostering bone calcification, associated with bone metastases, and reducing plasma sodium levels, respectively.

Such physiologic and totally non-toxic measures are preparatory to Laetrile therapy, of which Nieper writes as follows — "The specific non-toxic therapy of cancerous diseases began in my opinion only with the introduction of nitrilosides (Laetrile,, vitamin B-17) by Krebs and Krebs, Jr. The results achieved lately justify my assumption that the nitriloside (Laetrile) therapy is going to be, in the long run, the measure which can bring the cancer tissue best under some kind of acceptable control. It is an open secret that there exists in the USA for incomprehensible reasons — or rather very comprehensible ones — considerable opposition against starting nitriloside therapy. Whether private persons, authorities, or public institutions can morally afford such a behaviour remains to be seen.

It is obvious for me that the crisis situation in cancer research, sketched by me at the outset, and conditioned by an insufficiently developed and progressive kind of thinking, will develop into a conflict which can very heavily shake the societal and public structure. I am, nevertheless, doubtful on whether in such a quarrel scientific truth will be the loser, or whether the loser will not rather be the misguided children of an outdated system of thought.

Since cancerisation, i.e., the differentiation of trophoblast at the wrong time and/or place, signifies a latent danger for higher forms of life, it is quite possible that nature keeps ready preventative factors against such a development. Krebs and Krebs have been looking for decades into the question of which nutritional factors suppress the development of cancer in wild animals and in certain human groups, such as the Hunza of the Karakorum, who are nearly cancer free, in a statistically significant fashion, up to a very high age. They found that the so-called beta-cyanogenetic glycosides are responsible for this, which were also called nitrilosides by Krebs. Since the nutritional factor in question is preventive of disease, the nitrilosides are called vitamin B17, the "anti-malignancy-vitamin".

Nitrilosides are to be found in numerous wild grasses, in freshly sprouted cereal (wheat-grass) and in the kernels of pome fruit. Civilisation has more displaced nitriloside-supplying food.

The best known compound in the nitriloside group is amygdalin, which is also the easiest accessible. Amygdalin is highly effective in grafted tumors in animal experiments. Newer investigations, on which I shall still report at a later time, show that amygdalin is experimentally the more effective the slower a tumor grows. In this, it behaves exactly in an opposite manner to the now known cytostatics and carcinostatics. This property of amygdalin comes, however, very closely to clinical reality, which is that tumors grow very slowly in comparison to the grafted tumors in rodents. And so amygdalin is, as an example, effective in experimental tumors which can barely be influenced any more by cyclophosphamid (endoxan) or which, on the contrary, are even accelerated by it in their growth for the above mentioned reasons of immunological damage done to the cell's metabolism. New investigations at the Pasteur Institute have further shown that very high doses of amygdalin can neutralize the effect on the tumor in animal experiments, without otherwise producing toxic side effects. Or, in other words, extremely high doses of amygdalin hinder the process of metabolic utilisation of amygdalin. This knowledge is, for specific reasons, very important for the future.

Amygdalin is not effective as such as was shown in, among others, experiments on incubated emac-cells by Dean Burk. The HCN and benzaldehyde arising by decomposition of nitrilosides have together a

synergistic effect (Dean Burk) in damaging tumor cells. The thiocyanate generated through rhodanisation of HCH is, by virture of arising locally, again a carcinostatic principle which, after the latest observations, has possibly an even bigger importance than had initially been assumed (Nieper). Especially, in patients with liver metastases a conspicuous clinical effect can be achieved only if a very considerable supply of sulfur donors can be guaranteed, to the extent of at least 250 mg of S per gram of amygdalin. One will have to abandon the earlier Krebs theory of activation through beta-glucosidic fission in the body tumors. The effect of amygdalin in oral application is also much better when the tablets are cachetted to resist gastric juice. This speaks against the effect of an ingestion of rhodanates or of HCN from the decomposition of nitrilosides in the stomach, as had been assumed at first after the investigation of the conditions prevailing in sheep.

Apparently it is rather the nitriloside being locked into the cellular body and coming to develop only in the duodenum, which is responsible for the anti-malignant effect.

The principle of the beta-glucosidic fission in the release of the active substance is improbable also because of the negative result of the Daphnia experiment. May I refer, in this connection, to my earlier publication on amygdalin therapy, in this journal. Chance findings by Dean Burk have, however, opened completely new perspectives: namely that the glycolysis of tumor cells is *specifically* involved with the release of the active principle. Specific clinical experiences speak, in their turn, for a greater importance of an oxydative glycolysis than for an anaerobic one. (*Footnote:* *Clinical and radiological observations by *Nieper*. Experimental investigations by *Reitnauer* and *V. Ardenne* (Arzneimittelforschung, in press).)

Small tumors are substantially more influenced, both absolutely and relatively, than bigger formations. The time constants of the beginning of the effect in the patient are also shorter than the time constants for release of action under anaerobic conditions.

These remarks are intended to show only in an orienting manner how much we still are at the beginning of the clinical exploitation of nitrilosides. It is precisely because of this that I allot, of all the competing measures, including the immunology of tumors, the best prospect to bring the cancerous disease under an acceptable control, to the nitriloside therapy. The nitriloside therapy is the only medicinal cancer therapy which fulfills all the requirements for a definite clinical utility. Therapies which do not fulfill these conditions do not have, in my opinion, any opportunity for success in clinical and practical reality.

The conditions are:

1.) Oral applicability with undisturbed tolerance.

2.) Absolute non-toxicity at high therapeutic dosages, on continuous application for years and decades. Also, no damage to the liver.

3.) Dispensability of medical safety controls, e.g., absence of leukopenia, etc.

4.) Absolute absence of immuno-inhibiting effects under all conditions of application.

5.) Possibility of combination with any kind of hitherto known therapy, in particular that of X-rays and tele-cobalt irradiation.

6.) No interference, in the widest sense, with safety in surgery.

7.) Wide security margins against inexperienced application.

8.) Intravenous applicability, under special requirements.

I am perfectly aware that even a matured therapy can find a broad application for the benefit of the patients only if the medical community and the lay public are the most widely possible informed. Partly for this purpose we have taken action for the founding of an appropriate society.

On Dr. Hans Nieper's 8 points favoring Laetrile therapy over other therapy, we want specifically to mention his point 5) . . "Possibility of combination with any kind of hitherto known therapy, in particular that of X-rays and tele-cobalt irradiation" . . This does not constitute a recommendation of radiation. It simply means that Laetrile does not interfere with the action of radiotherapy — though aside from the skin and superficial cancers radiotherapy is not advised. American students of Laetrile are particularly opposed to radiotheraphy as being unphysiological and generally having a greater potential for harm than for good . . Even in skin or superficial cancers they favor the escharotic application of such radiomimectic chemicals as methotrexate over radiation itself. There are some dermatologists particularly skilled in such so-called chemosurgery.

On the other hand, the mechanical resources of surgery in some instances are often life-saving in combination with Laetrile therapy. We have demonstrated clinical arrestments of cancer, of years standing, that surgery alone or Laetrile alone could not have saved; but were saved through the judicious combination of the two.

It is not necessary to comment at length upon Nieper's questioning of Kreb's original and possibly simplistic explanation of Laetrile action through selective hydrolysis of the molecule by the enzyme beta glucosidase . . newer data have tended to reaffirm most students of the problem that the basic beta glucosidase hypothesis is a valid one for explaining the action of Laetrile. However, it will be noted that even where there is a complete unanimity of the clinical effectiveness of Laetrile in therapy and prophylaxsis of cancer we still find minor differences among various students as to the explanation of the specific mechanism of its action.

Phase I.

By Hans A. Nieper

Cancer research has, for the last 15 years, been in a state of crisis which at present seems even to be increasing in intensity. The reason for this crisis lies, in my opinion, in an insufficient grounding of numerous cancer researchers in the categories of modern scientific thought and in our lacking the capability to suitably handle complex theoretical objects with strongly polyfactorial characteristics. It appears increasingly that it is rather useless to pursue experimental cancer research for the production of tube-like fields of vision without learning about the theoretical exploitation of an observational result from the theoretical physicists of the early twentieth century, from the relevant philosophers of the nineteenth century, or even from the contemporary methodologists of science.

It pertains to the exercise of modern research that the researcher be informed on pertinent previous studies. This does in no way happen through a simple method of cataloguing or enumeration but only through subtle 'comprehension' along a self-elaborated logical path. Preliminary studies must then be understood, in the strict sense, historically, as only in this fashion their ordering and correlation to one's own activity is possible.

How could it otherwise be understood that in cancer research results and observations long ago known can be presented, over and over again, as new, and be accepted and praised by an extensive authoritative body which does not know the existing contingencies?

One example of this is the description of the C-particle from human tumor tissue by DMOCHOWSKI and PRIORI. Moreover, this particle is even being addressed as a virus. Not only that DMOCHOWSKI has previously (1968) described himself such particles from human mammary carcinoma, but also SANFELICE and RONCALI have reported in 1898 in the ZENTRALBLATT FUER PARASITENKUNDE on precisely such particles. That we are dealing here not with a virus but with an auto-reproductive agent having fungic properties — as well in regard to its morphological cycle as to its metabolism — has been completely clarified in the twenties and thirties of this century. Recently this recognition has been confirmed by Mrs. LIVINGSTON's work in San Diego.

The fungic nature of the C-particle should have been considered proven, at the latest, by BEARD's communication that C-particles have a high phospholipid (Malignolipin) and only a minimal nucleic acid content. The origin of the ABC-particles in the mitochondrial membrane, which I have described in 1957, has also been resurrected in a whole number of papers which, again, do not refer to each other. THOMAS in Paris has, in an impressive piece of work, reduplicated the life work of V. BREHMER and that of GLOVER and represented again, in an electronoptical fashion, just about the whole already known morphological cycle. In addition, THOMAS' investigations, but also those of several other authors, show that the "Leucose-agent", "Rous-agent", "Bittner-Mouse-Mammary-Carcinoma-agent", the same in man (also investigated in Houston!), and several other special forms of "cancer viruses", which are in reality altogether only special forms of the oncogenic agent, which can develop A, B, and C-forms, and which do enter the mycetozoic cycle. It occurs, however, quite often that a viral factor of a specific kind can play a role in the agent. The expression "helper virus" is occasionally used for such an additional factor in the Rous agent. Besides, specific particularities of an oncogenic agent are a normal occurrence depending on the origin of the cell tissue. HAMAZAKI, for example has investigated this. He fed rats tissues of human stomach carcinoma. The rats then developed a leukemia the agent of which, however, still maintained the immunological properties of the human stomach tumor.

That the number of studies demonstrating agents, respectively C-particles, in tumors induced by chemical carcinogens has already become very big does not need a special mention. FRANZ BUECHNER has already pointed this phenomenon out before 1905, in his lectures, Nothing has been changed in the findings of WYBURN-MASON, established eight years ago, saying that only first generation, freshly induced benzopyrene and metallodextrane tumors are devoid of the agent. These tumors are also the only ones which do not form the subcellular LDH-forming — i.e., glycolytically active — Riley agent. It is, moreover, strange that until today no experimental virologist has been found who — in conformity with the publication — would have applied, as WYBURN-MASON did, the thermotropy procedure to the extraction of subcellular, autonomous structures. PAUL EHRLICH writes, around the turn of the century, that this procedure is already known. It is an old standard method of bacteriological and virological preparation; waiting for the autolysis is only an insufficient substitute.

THOMAS did not know V. BREHMER, GLOVER, CLARK or WYBURN-MASON, just as, on the other hand, DMOCHOWSKI obviously does not know about THOMAS or about the consequences of his work. And so, good tidings can be gathered from new academic work that the "particles" should be sensitive to a lowered pH; it can be heard from Essen that autolysing or aging tumor cells are "releasing virus" — a finding known for forty years, photographed by SEYFARTH and myself, with the subtle distinction that the released virus is no virus.

There is no end to the senseless duplication and the blind roaming about. In the end, of course, it is not the publishing researchers who are to be blamed for this mess, but the system which is incapable of sufficiently developing associative activities of higher cerebral functions. But who is to blame for this sytem of practicing biological science? Certainly also those institutions which mean to be of substantial use to cancer research through "central documentation centers". After all, what one possesses in black on white has, as a rule, not yet been integrated into an adequate system of thought. A little bit of systematic scientific all-round education and the knowledge of the most important languages just are part and parcel of a researcher who intends to raise himself past the handicraft type of laboratory work.

Let me now slacken the tenor of the text to a duller and, consequently, more serious norm: the A, B, and C-particles are of course the well known states of the subcellular oncogenic agent which possesses philogenetically an atavistic character with all the properties pertinent to it. There is, according to several newer papers, no doubt any more about its origin in the cytoplasmic structures. US virologists have, ignoring these things, given the sporal form the designation A, sporangic formations are designated as B – their bursting was described, moreover, in 1969 independently by two virologists who were ignorant of pertinent earlier studies – and the C-particles are the known polymorphic round forms which arise through the exit of the sporal lipoid-nuclein-nucleus through the cellular membrane, likewise obtaining a double contoured lipoid-containing outer membrane. Since these subcellular formations are responsible not only for the cancerous disease itself (e.g., hemolysis) but can also undoubtedly exert a transmission of infection, it is proper, understandable taboos not withstanding, to deal a little bit with the infectious transmission of the cancerous disease through the oncogenic agent. The higher morbidity for personnel nursing persons suffering from cancer, in particular those affected by cancer of the skin, and the surviving conjugal partners of persons suffering from cancer, to which HEITAN had already pointed 15 years ago, has not yet been pursued any further. Anyway, it was reported in 1968 from California that people, who live together with tumor-carrying dogs, present about 85% more malignomas than people with tumor-free dogs. The relation between dogs with melanomas at their heads to human cancer disease was even much more remarkable. Two years ago MALMGREN and MORTON reported on some very revealing findings from virus-resp. agents in 80 patients with malignant osteo-sarcomas. DEAN BURK, from the same institute as the above authors, viz. the National Cancer Institute in Bethesda near Washington, communicated to us privately that 79 out of these 80 patients held dogs, whereas in a normal distribution only 13 out of 80 should have had to hold dogs.

According to DEAN BURK's communication the authors were initially startled by this information. One should, at any rate, know these things in order to arrive at a hygienic legislation on dogs, long overdue as it is. More recently it is also being pointed out that immunological peculiarities of the infectious particles in cat leukemia lead to apprehensions lest there be an infectious transmission to man.

HORN and HORN report on a father whose son and two nephews contracted renal carcinomas within the delay of five years. I myself am following two families, in which 2 children of the same father, after he had been taken ill of a hypernephroma, contracted pulmonary and brain tumors; in another case a 36-year old woman contracted fulminating multiple malignant tumors of the lung after she had nursed her husband who had fallen ill of renal carcinoma. HORN and HORN assume a transmission of infection.

It becomes ever more probable, for various reasons, that the phospholipid in the particle is a substantial informant of the infectious process. Investigations in the USA and in India on phospholipases point into the same direction. For this reason lipid-soluble thiocyanates can have a very substantial function in the neutralisation of such infectants. I shall return to this later.

This particular aspect, which is of a very practical importance, has also been given prominence recently by the communication of LAWS (Baltimore): the typically lipid-soluble DDT inhibits cancerisation not only in workers in chemical industry with a remarkable degree of protection, but has also an inhibitory effect on transplantable mouse tumors which is, however, smaller than that of amygdalin. Even an atmosphere of carbon disulfide (CS_2) seems, judging by my own work, to largely protect industrial workers from cancer, for the above-mentioned reasons.

More recently another clinically secured observation must be mentioned here: the statements made by RASSIDAKIS, according to which persons suffering from schizophrenia have an emended mortality of exactly 1/3 of that of the normal population, have been perfectly confirmed in England and in the Soviet Union. XALABARDER has made the discovery around 1956 during electron-optical investigations on thrombocytes that these exhibit very strange contours. During our common investigation with the electron microscope of the oncogenic agent this appeared again. At the same time HEATH was able to make the anti-ganglioside (phospholipid)-antibodies for the first time a probable contender for the causation of schizophrenia. I have visited him in 1970 in New Orleans and looked myself at the corresponding fluorescence labellings. One can be safe in assuming, in schizophrenia, the presence of aggressive antibodies against phospholipids, which also

explains, after what has been said above, the lesser frequency of cancer in schizophrenics.

The role of real viruses, which do not multiply, in contrast to the oncogenic agent, on inanimate media, and which have a completely different chemical constitution, has to be judged in a fundamentally different manner in the induction of cancers. They can, in the guise of epidemic infections from the outside world, produce malignant processes, but this is not an infection proceeding from a tumor carrier. Four years ago in Atlanta a very revealing study was carried through on a massive, obviously infectiously conditioned accumulation of carcinomas of the colon in black people, which was explained by a genital transmission of the herpes simplex virus. Indications have multiplied in the last years that in carcinomas of the colon herpes viruses seem to be an essential initiator. Even influenza and adeno viruses can, according to numerous available evidence, be substantial initiators of malignancy. I have myself seen on various occasions accumulations of multiple lung tumors arising when a bronchogenic viral infectant meets a familiar, auto-immunologically conditioned "asthma-like bronchitis" or a beginning dystrophy of the lung of the HEILMEYER type. It must be noted in this regard that the concepts submitted several years ago by DICK in Belfast, according to which bronchial carcinomas in smokers arise only through the communication of a bronchitic auto-immunological process, have found a weighty parallel in newer work on the genesis of asbestos cancers. It is also entirely possible that only the — omnipresent — viral effect transforms the smoker into a person suffering from cancer. Recently Russian researchers have shown experimentally that a latent chronic intoxication with urethanes, which in itself does not cause any lung neoplasms, does predispose to lung tumors, when an influenza or adeno virus hits such animals. That a transcriptase, revertase, from RNA to DNA, had to exist was an obligatory requirement for anyone recognizing phylogenesis as the grammar of biology. The proof of this enzyme by TEMIN and SPIEGELMAN makes certainty out of the theoretical assumption.

It was the Russian BAZIKIAN who was able to prove again the negative correlation of cancers of the stomach to the magnesium content of drinking water. The tumor inhibiting effect of magnesium chloride in animal experiments, done by the same author, is also highly significant. This had already been proven extensively by DELBET and ROBINET between 1922 and 1944, and equally by REDING. I have myself taken random samples in 1953 and 1955 in France with the help of various very cooperative city administrations, and obtained the same result.

In order to lead over now to the topic of tumor immunology let me turn first of all toward surgery which, it is said, has largely exhausted

its possibilities. Some years ago two meetings of surgeons took place, independently of each other, in Graz and Chicago, during which even older surgeons reported on the remarkably long term and occasionally definitive survival of cancer patients in which visible metastases had been electro- or heat-coagulated "ex juvantibus" during the operation. Well, it is known from various experimental work that proceeding in this fashion can positively have the effect of a protective vaccination because antigenic material can be released through the heat. It is therefore imperative, in my opinion, that this possibility be constantly thought of in every operating room, the more so as it certainly does not constitute an encumbering commitment. "What is most difficult to see? That which is right in front of your eyes!"

That even the cryosurgical method of freezing the carcinoma of the prostate is able, through the release of immunological mechanisms, to bring far away metastases to vanish, has been confirmed several times over at a relevant congress in 1969 in Torino. Even this is ultimately a clinical extrapolation of the old experiments DOMAGK and HACKMANN did, when they produced, by breaking up cells of the Ehrlich-ascites-carcinoma of the mouse through cold, a protective vaccine against this carcinoma. That cancer is more common in those people suffering primarily of an immuno-insufficiency (non-infectious diathesis) has been proven everywhere, since the investigations of HENSCHEN in Basel, 25 years ago. Empty anamnesis is typical for a person suffering from cancer. In the meantime it has become known from several publications — there were two at once, following each other, in the JAMA — that immuno-inhibiting measures connected with central immuno-suppression, for example in transplantation surgery, are leading to increased frequency of tumors in the receptors. Two other very important previous findings and suppositions were furthermore supported by the observation of this phenomenon:

First, it seems more and more, as the years go on, that the about 15 year old opinions of ELIAS in Chicago, to which I myself am also very sympathetic, are being confirmed. SEYFARTH is of the same opinion. ELIAS thinks that the function of the subcellular agent, and not only the spreading of the malignant cells, is an essential one in the realisation of metastases. The authors on frequency of malignomas after transplantations (from organs of cancerous donors) were unfortunately not too well versed oncologically in order to shed light on this question, but the facts reported are very much speaking for it. In addition to the old studies by ELIAS the fact that experimental tumors do not metastasize for as long as RILEY and WYBURN-MASON negativity exists speaks for an agent-motivated metastasis. Italian authors have furthermore reported recently very reliably on the production of histologically typical Yoshida sarcomas from Yoshida agent.

Perhaps the histological difference of the metastases in regard to the primary tumors also belongs under this heading, but this is beyond my competence. Anyway, the confirmation of ELIAS' conceptions would open a decisive new perspective on the medical therapy of cancer.

Second, work on the immuno-suppressive ALS (anti-lymphocytic serum) has shown that frequently malignant lymphomas can be expected. This points very much to a mechanism of specific antigen (equals organiser) destruction in the lymphocytes, or the tissue in which they originate, by ALS, so that here again the principle of the malignant process, described first by WEILER, becomes apparent. The experience made with ALS stands simultaneously for the process of malignancy through auto-immuno-aggression, which in my opinion is the most important one in clinical reality.

It was left for the amiable and praiseworthy Swiss courage, namely that of BRUNNER in Bern, to report on a long term Endoxan therapy has a negative effect on the freedom from relapse after surgery of bronchial carcinoma. This means that it is often better to do nothing than to give Endoxan. I once was capable myself to increase the growth rate in slowly growing grafted tumors in rats by treating them with Endoxan. The damage done to the immunological system was weightier than the curative effect on the tumor. Besides, it is shown here that Endoxan and all other cytostatics, with the exception of a few anti-metabolites, is practically ineffectual in slowly growing tumors, where they do damage to the immunological reaction of the host. Such cytostatic substances are only effective in fast growing tumors. The situation is exactly reversed in the nitrilosides, yet to be discussed. Slowly growing tumors are, in effect, the clinical reality. Even very slowly growing experimental tumors belong, from the clinical point of view, still to the class of fast growing ones. This truism was not heeded in the experimental screening centers in the USA and other civilized countries. The radical criticism of this failure, touching the system itself, which ULLMAN and I started more than ten years ago, is now slowly yielding its harvest. In the most recent past SANDBERG and GOLDIN reported an experimental Slow Tumor, exhibiting the approximate thymidine uptake of human carcinomas, and which is supposed to be equated with them. Applied to this tumor, the conventional cytostatics are a nearly complete failure. The Pasteur institute possesses a similar experimental tumor which is being used for testing nitrilosides.

Some programmatic points on the immunology of cancer, which have been published lately, are very remarkable: first, it is now "officially" proven that abundant food for the person suffering from cancer leads to the formation of factors inhibiting the immunological tumor defense (DAVID ROSE), so that scanty nutrition, and even

sub-nutrition, becomes immunologically expedient. Two, a group in Minneapolis reported that the detaching of the mucoid layers on the phospholipid of the cancer cell and on the agent by neuraminidase (extracted from Vibrio Cholerae) releases the most effective tumor antigen which has been found as yet. The vaccination results are very impressive, and a genuine possibility arises here for a serious cancer vaccine. Although this has been known for a long time by the researchers occupied with dark-field diagnosis, there is a precise and applicable progress here. A further very essential measure for indirect immunotherapy, which has to do with an amelioration of the available supply of ATP, will be discussed further below.

Besides, we shall have to free ourselves of the concept that there is such a thing as "cancerous" and "cancer-free" man. Even more nonsensical is the idea that there exists a radical cancer surgery in the sense of complete deliverance of the organism. The end result of the surgical therapy of cancer is solely of a statistical kind and results from the post-surgical balance between host and disease. Findings by BERGE and LUNDBERG are remarkable which show, through very intensive post mortems of 11,000 deceased persons, that 44,1% malignomas were discovered whereas only 26,3% of those persons were previously considered as suffering from cancer. In a hypothetical all-over microdissection perhaps 80—90% of the deceased would have been cancer carriers. It is also remarkable that one researcher working on sputa was able to find tumor cells cytologically, but he succeeded in proving a beginning bronchial tumor only 7 years afterwards. And a tumor weighing one gram has already divided through more than 40 generations, whereas 20—30 more generations are enough to seal the fate of the patient.

We shall have to get accustomed, when treating cancer, to think in extremely long time spans. A distinguished New York oncologist expressed to me still in 1970 his opinion that an observation time of 60 days in the application of a carcinostatic was satisfactory to him! We shall have to equally become accustomed to the fact that a genuinely progressive early diagnosis of cancer — DEAN BURK and others reported on this two years ago — will show positive results in apparently healthy persons who will not appear clinically as tumor carriers during their life time.

All this points toward the need for using only measures effective over long periods, that is, *non-toxic* ones, in the future control of the cancerous disease. From the whole big group of cytostatic substances only several, at best, weakly aggressive anti-metabolites with delayed action will ultimately remain, in my opinion. For the rest the medically therapeutic field will belong to immunology and to the non-toxic anti-malignancy substances.

I do not want to make any further comments here on immunological cancer therapy. It might still be mentioned, though, that the release of the antigens from plastered over layers of mucoid — in particular that of malognolipin — which is decisive for the unfolding of the immunological mechanism, can be effectuated only extra-corporeally through neuraminidase. The following measures or reactions have a mucoid-loosening action in the patient: 1). X-ray or tele-cobalt irradiation. There is then an increased excretion of glucosamin, and also of galactosamin and mannosamin. 2). Through acidification, with a lowering of the pH in morning-urine, e.g., through the K-P-complex Gelum oral rd. 3). Through appropriate nutrition interspersed with phases of fast. 4). Through ozone, intravenously. The mechanism is probably identical to that in X-ray irradiation, i.e., through the action of OH-radicals. 5). Through proteolytic enzymes, such as the Wobe-Mugos one. 6). Through some not yet clarified mechanisms, among which immunoreactions. 7). Through desodification with lithium-succinate. 8). Through Atebrin, Resochin. 9). On breakdown of the buffer system in the cancerous person and formation of the prefinal acidosis (lactic acid) and pre-mortal drop of the blood pH there is an abrupt atrophy of the mucoid covers, including the B- and C-forms. (Apparently not known to any cancer virologist but well known in the dark-field diagnosis.) 10). The most significant method in the practical application for diminishing the immuno-blocking mucoid covers is finally the continuous treatment with herparinoid substances, around 50,000 to 70,000 U per week. We have been treating a group of patients for two years with Eleparon in combination with Amygdalin. The results are spectacularly improved over simple treatment with Amygdalin. I shall communicate details on this in the second part of my report.

Besides, I must mention that E. T. Krebs, Jr., about who I shall still speak, is of the opinion that the strong development of mucoids, typical for malignant material, belongs to the phylogenetic atavisms which are characteristic of malignant behaviour. I refer in this connection to some of my earlier publications on this topic. There are a series of cogent proofs for the soundness of KREBS' assumption. It can have big practical consequences, for example in the correlation to gravidity and immunological block through mucoid covering in the trophoblast.

The non-toxic chemotherapy of cancer is only in its beginnings. Part of the reason for this is that in official research the necessity for long-range medicinal therapy has been underestimated and toxical side effects in manipulating chemotherapeutic concepts so far have been accepted too thoughtlessly. De facto, however, even small toxic side effects have a declassing effect on cancer medicines. I do not understand, in principle, why so much work and money have been put into researching alkylating substances, under misleading conditions of

experimentally testing on rapidly growing grafted tumors, to boot. Following a simple theoretical train of thought in a consequent manner should force one to give up such a program as useless from the very beginning.

There are a number of longer known methods for treating cancerous disease with non-toxic methods. The most successful of the older procedures, and at the same time the best secured one experimentally, is certainly the mistletoe therapy. Let me recommend to those interested VESTER's new publications on this topic.

In efforts . . . . (piece missing: perhaps: . . . diminish the toxicity of cancer therapy, Transl.) the hyperthermy therapy (LAMPERT), which VON ARDENNE developed to a multi-step cancer therapy, has also to be included. Despite of much criticism it seems to be certain now that this concept is becoming clinically practicable with good results. By its nature, however, it is a short-time therapy which, to be sure, could uprate even more the concepts of non-toxic, long-time therapy through its results. In the Federal Republic it is OLLENDIECK who has acquired great merits in using the hyperthermy therapy.

A series of measures for medicinal ways of influencing the host organism and the terrain on which the cancerous disease develops, as well as the tumor, are certainly important. The amelioration in making ATP available without which there is neither an optimal immunological activity nor an optimal liver- or undisturbed heart fuction, has to be included here. The means of choice to achieve this is K-Mg-aspartate which, according to NAKAHARA, very strongly activates the formation of ATP.

The importance of these relations has been, until recently, much underestimated. I have to remark in this regard that I have developed in 1957, together with Dr. KOEHLER's help, the Mg-K-aspartate for the treatment of the terrain in cancerous patients. The oustanding importance of this substance for cardiology, which has expressed itself in the meantime in roughly 2000 publications throughout the world, started but in 1958. NAKAHARA reported in the early 1960s his experimental results on the process of making ATP available. As can be seen in figure 1, the results speak for themselves.

Finally, in 1971 a communication from KRONBERGER and FINK in Graz appeared, which can scarcely be rated high enough. Whereas KRONBERGER's own investigations as well as indications in the world bibliography give a 4 year survival rate figure between 20% and 42% after surgery on carcinomas of the stomach and the intestinal tract, a rate of 83%!! can be established if the patients are continuously treated post-operatively, and without interruption, with K-Mg-aspartate. The number of cases observed is 103. This communication would seem nearly unbelieveable had not CHANDRA in Frankfurt reported

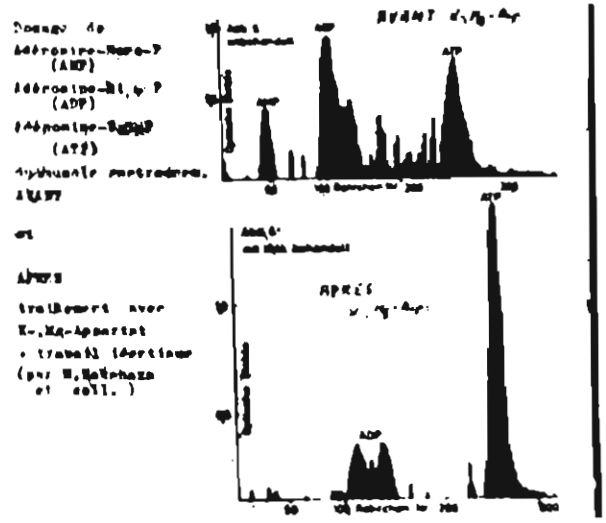

Fig. 1: Effect of K-Mg-aspartate on the available pool of ATP

very abundantly on the very strong increase in the activity of immunocompetent cells and formation of antibodies by them brought about by cyclical AMP. The treatment of cancer patients with K-Mg-aspartate and possibly also with additional cyclical AMP has become for us a condition sine qua non. It is, furthermore, peculiar that cancer patients show practically always a deficit of zinc in their total blood. Zinc is, however, absolutely necessary in order to keep the cellular immunity going, as the lymphocyte desaminases function only in the presence of zinc. This is also the reason why the zinc concentration of the spleen is much higher than in other organs, being surpassed only by sperm. For this reason my cancer patients obtain from me, if possible, Zn-2-aminoethanol-phosphate (Zn-EAP), a zinc carrier, which leads to an increase in the lymphocyte count in cancer patients, where it is mostly lowered. Zn-EAP probably very much ameliorates, in addition to this, an insufficient production of insulin. We shall further report on this in the future. Persons suffering from cancer nearly always show, on analysis of their whole blood, a considerable excess of sodium. The sodium is mostly enriched intra-cellularly, which is a consequence of metabolic damages to the cell's energy metabolism. The ingress of sodium itself leads to a further metabolic insufficiency which can express itself in immunological debility, inappetence, adynamia, etc. The displacement of superfluous sodium in the cancer patient is therefore essential. This is best achieved with Li-succinate which possesses a better lipid affinity than Li-orotate or Li-citrate. It is also possible for the same reasons to dry out malignant effusions in body cavities with Li-succinate. Toxic side

effects are practically nil, as long as doses of 400 mg per week are not exceeded and the whole blood is occasionally monitored spectrometrically. The research on sodium displacement (desodification) has not yet been concluded, and we shall report on it later. Just as important as the supply of K and Zn under conditions of active transport in the form of aspartate or orotate, is the supply of chloride, which is mostly being treated in a rather stepmotherly fashion. Infusions with an excess of chloride or oral application of chlorides, which are not Na-chlorides, are appropriate. The supply of iron should come about only in the form of active transport substances, first of all as the orotate (DURANT), or at least as Fe-aspartate (Spartocine).

Within the frame of our investigations on the active transport of minerals we concerned ourselves with finding out whether it is possible to influence bone decalcification due to cancerous disease in general, to bone metastases in particular, and as delayed damage from X-ray irradiation. The achieved results with Ca-orotate and with Ca-2-aminoethanol-phosphate, together with Mg-2-aminothanol-phosphate, are quite satisfactory. Using this method it is even possible to recalcify bone metastases, as I have already reported several times and for several reproduced cases. The treatment of the diseased terrain, exhibited here, together with an acidifying diet, cleaning out of foci and bodily exercise is a basic program more or less undergone by each of my cancer patients. Adjustment of the intestinal flora and treatment of heart and liver are usually an additional feature.

The specific non-toxic therapy of cancerous disease began in my opinion only with the introduction of nitrilosides by KREBS and KREBS, Jr. The results achieved lately justify my assumption that the nitriloside therapy is going to be, in the long run, the measure which can bring the cancer disease best under some kind of acceptable control. It is an open secret that there exists in the USA for incomprehensible reasons — or rather very comprehensible ones — considerable opposition against starting the nitriloside therapy. Whether private persons, authorities, or public institutions can morally afford such a behaviour, remains to be seen. It is obvious for me that the crisis situation in cancer research, sketched by me at the outset, and conditioned by an insufficiently developed and progressive kind of thinking, will develop into a conflict which can very heavily shake the societal and public structure. I am nevertheless doubtful on whether in such a quarrel scientific truth will be the loser, or whether the loser will not rather be the misguided children of an outdated system of thought.

Since cancerisation, i.e., the phylogenetic-atavistical becoming autonomous of organ tissue, signifies a latent danger for higher forms of life, it is quite possible that nature keeps ready preventative factors against such a development. KREBS and KREBS have been looking for

decades into the question of which nutritional factors suppress the development of cancer in wild animals and in certain human groups, such as the Hunza of the Karakorum, who are nearly cancer free, in a statistically significant fashion, up to a very high age. They found that the so-called beta-cyanogenetic glycosides are responsible for this, which were also called nitrilosides by KREBS. Since the nutritional factor in question is preventive of disease, the nitrilosides are called vitamin B17, the "anti-malignancy-vitamin".

Nitrilosides are to be found in numerous wild grasses, in freshly sprouted cereal (wheat-grass) and in the kernels of pome fruit. Civilisation has more and more displaced nitriloside-supplying food.

The best known compound in the nitriloside group is amygdalin, which is also the easiest accessible. Amygdalin is highly effective in grafted tumors in animal experiments. Newer investigations, on which I shall still report at a later time, show that amygdalin is experimentally the more effective the slower a tumor grows. In this it behaves exactly in an opposite manner to the now known cytostatics and carcinostatics. This property of amygdalin comes, however, very closely to clinical reality, which is that tumors grow very slowly in comparison to the grafted tumors in rodents. And so amygdalin is, as an example, effective in experimental tumors which can barely be influenced any more by cyclophosphamid (Endoxan) or which, on the contrary, are even accelerated by it in their growth for the above mentioned reasons of immunological damage done to the cell's metabolism. New investigations at the Pasteur institute have further shown that very high doses of amygdalin can neutralize the effect on the tumor in animal experiments, without otherwise producing toxic side effects. Or, in other words, extremely high doses of amygdalin hinder the process of metabolic utilisation of amygdalin. This knowledge is, for specific reasons, very important for the future.

Amygdalin is not effective as such as was shown in, among others, experiments on incubated EMAC-cells by DEAN BURK. The HCN and benzaldehyde arising by decomposition of nitrilosides have together a synergistic effect (DEAN BURK) in damaging tumor cells. The thiocyanate generated through rhodanisation of HCN is, by virtue of arising locally, again a carcinostatic principle which, after the latest observations, has possibly an even bigger importance than had initially been assumed (NIEPER). Especially in patients with liver metastases a conspicuous clinical effect can be achieved only if a very considerable supply of sulfur donors can be guaranteed, to the extent of at least 250 mg of S per gram of amygdalin. One will have to abandon the earlier KREBS theory of activation through beta-glucosidic fission in the body tumors. The effect of amygdalin in oral application is also much better when the tablets are cachetted to resist gastric juice. This speaks

against the effect of an ingestion of rhodanates or of HCN from the decomposition of nitrilosides in the stomach, as had been assumed at first after the investigation of the conditions prevailing in sheep. Apparently it is rather the nitriloside being locked into the cellular body and coming to develop only in the duodenum, which is responsible for the anti-malignant effect.

The principle of the beta-glucosidic fission in the release of the active substance is improbable also because of the negative result of the daphnia experiment. May I refer, in this connection, to my earlier publication on amygdalin therapy, in this journal. Chance findings by DEAN BURK have, however, opened completely new perspectives: namely that the glycolysis of tumor cells is *specifically* involved with the release of the active principle. Specific clinical experiences speak, in their turn, for a greater importance of an oxydative glycolysis than for an anaerobic one. (*Footnote:* *Clinical and Radiologic Observations by *Nieper*. Experimental Investigations by *Reitnauer* and *v. Ardenne* (Arzneimittelforschung, in press).) Small tumors are substantially more influenced, both absolutely and relatively, than bigger formations. The time constants of the beginning of the effect in the patient are also shorter than the time constants for release of action under anaerobic conditions.

These remarks are intended to show only in an orienting manner how much we still are at the beginning of the clinical exploitation of nitrilosides. It is precisely because of this that I allot, of all the competing measures, including the immunology of tumors, the best prospect to bring the cancerous disease under an acceptable control, to the nitriloside therapy. The nitriloside therapy is the only medicinal cancer therapy which fulfills all the requirements for a definite clinical utility. Therapies which do not fulfill these conditions do not have, in my opinion, any opportunity for success in clinical and practical reality.

The conditions are:

1.) Oral applicability with undisturbed tolerance.

2.) Absolute non-toxicity at high therapeutic dosages, on continuous application for years and decades. Also, no damage to the liver.

3.) Dispensability of medical safety controls, e.g., absence of leukopenia, etc.

4.) Absolute absence of immuno-inhibiting effects under all conditions of application.

5). Possibility of combination with any kind of hitherto known therapy, in particular that of X-rays and tele-cobalt irradiation.

6.) No interference, in the widest sense, with safety in surgery.

7.) Wide security margins against inexperienced application.

8.) Intravenous applicability, under special requirements.

I am perfectly aware that even a matured therapy can find a broad application for the benefit of the patients only if the medical community and the lay public are the most widely possible informed. Partly for this purpose we have taken action for the founding of an appropriate society.

SUMMARY

A number of new aspects of changes in our knowledge of cancerous disease is critically outlined. Cellular and infracellular facts of malignancy are discussed with special reference to problems of immunoresistance, enhancement by mucoid layers, and infracellular spread of the disease.

It is outlined in detail why a long-time therapy (unlimited in time) of cancerous disease is imperative and to which criteria it has to obey. All so far known synthetical or toxic cytostatics are more or less useless for such propose, their testing in grafted tumors proved to be misleading in respect to their clinical value. It is outlined that according to the present knowledge only the nitriloside therapy seems to be promising as chemical long-time therapy of cancerous disease. It alone complies with all the imperative needs. Additional devices of immunotherapy, the interruption of immune-blocking (mucoid-solving heparinoids; and the support of the conditioning of the host is listed in short but relatively completely. This includes active zinc transport for the enhancement of lymphocytic desaminases, the application of calcium diorotate for the recalcification of bone metastases and of the prevention of such, and the medication of K-Mg-aspartate for increasing the ATP-pool.

Eine ausgewählte Literaturaufstellung wird am SchluB von Teil II gegeben.

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(Forts. folgt)

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