(medullary or myelin sheath). This knowledge represents a solution to the puzzle of how multiple sclerosis actually develops. Naturally, there are still a number of questions which have to be answered. Considering more recent knowledge, however, therapeutic strategies have been developed which are now providing the first positive results.

Tumorous diseases

Cancer therapy

Professor Karl-Heinz Bauer, president and founder of the Cancer Research Center in Heidelberg, German postulated already more than 30 years ago that cancer is a localized disease and that a treatment must therefore be applied directly against this local illness. Anyone who believes that the body has an endogenous defensive system active against cancer and that cancer is a systemic disorder can only be considered to be a charlatan or "quack". Many of his colleagues at that time responded to him with claims that, "Cancer and chronic inflammatory diseases develop when the defensive mechanisms of the organism are weakened. An effective therapy must eliminate these disturbances and improve the body's defensive conditions." The knowledge gained about immunology, however, has forced scientists to give up the idea of treating cancer as a local disease. Nevertheless, this does not mean that surgery, chemotherapy and radiation therapy have to be abandoned generally in oncological treatment.

The two contrasting positions, however, clearly demonstrate the area of conflict in which cancer therapy is found and make clear why there are two different therapeutic strategies in oncology. The surgical, chemotherapeutic and radiological measures with the goal of local tumor destruction stand in contrast to those measures for strengthening the defensive powers of the organism. Today, these two therapeutic strategies are increasingly being combined in an integrated therapeutic concept. In the case of cancer, however, everything is very different, very slow-moving and very arduous. One must constantly be reminded of not being too hopeful. This is true for the use of proteolytic enzymes in the treatment of cancer as well. Nevertheless, there are a number of areas in which the use of an enzyme therapy is clearly seen to be very valuable and has proved to be effective.

Paul Ehrlich (1854–1915), a famous German physician and scientist, already established a theory at the beginning of the century that the

development of cancer is dependent on the results of the "fight" between the tumor cells and the immunological system. The strength of the immunological system and the particular characteristics of the tumor cells are responsible for the outcome of this conflict. These characteristics include the malignancy of the tumor or its tendency to metastasize and to penetrate into other tissues, as well as its capability of disguising itself from the immune cells. The recognition of tumor cells by the immunological system is a very difficult procedure. It should not be forgotten that tumor cells are derived from the healthy, endogenous cells of the organism. For this reason, it may be possible that the antigenic structure of a tumor cell differs only insignificantly from that of the healthy cells – a cause for problems with the defensive system. In spite of these difficulties, and according to the knowledge presently available, the healthy immunological system is nonetheless able to recognize and to destroy the great majority of tumor cells.

As a logical consequence, there are two modes of therapy for the immunological treatment of cancer. Attempts are made both to increase the recognizability of the tumor cells for the immunological system (that is their immunogenicity) as well as to strengthen and stimulate the various parts of the immunological system. Proteolytic enzymes are able to play a role in both aspects of this therapeutic strategy. They increase the immunogenicity of the tumor cells and, at the same time, support the immunological system of the patient at various levels.

Effects on the tumor cells	Effects on the immunological system
Changes in the coating substances and changes in the cell surfaces (increase in the immunogenicity)	Degradation of circulating immune complexes (elimination of the "blocking factors")
Exposure of the tumor cell antigens (increase in the immunogenicity)	Increase in phagocytosis (elimination of the "blocking factors") Activation of the macrophages and NK cells (direct attack against the tumor cells) Secretion of cell messenger substances (TNF, interleukin)
Decrease in the adhesive powers	Inhibition of the adhesion molecules important for metastasis Increase in the degradation of fibrin

Table 5: Effects of systemic enzyme therapy on the tumor cells and on the immunological system

The oncological indications for a systemic enzyme therapy are initially seen in the primary (preventing development) and secondary (preven-

tion of recurrency) tumor prophylaxis. Enzymes are able to maintain the state of health of high-risk patients and, following a successful initial therapy, serve to inhibit a recurrency or the development of metastases. The immunoregulatory and immunoactivating effects of an enzyme therapy, however, are useful during all phases of a cancerous disease.

A weakened immunological system must also be supported in order to reduce the extent of existing tumorous masses as far as possible. Depending on the type of tumor, this can be performed by way of surgery, chemotherapy or radiotherapy (here, the oncologist must select the most promising method). Some tumors respond better to chemotherapy, while others are more sensitive to a radiation therapy. At the same time, attempts must be made to reduce the adverse effects of this aggressive therapy and to mobilize the defensive powers. Proteolytic enzymes are successfully applied together with chemotherapy and radiotherapy in order to reduce the adverse effects.

The older the patient, the higher the risk

The development of cancer is a process which involves the cooperation of many factors. Included among these factors are the genetic disposition (heredity), the living conditions (nutrition, exposition to dangerous substances, exposure to such radiation as, for example, UV radiation), infections, the psychological state of the patient, as well as the patients' age.

It is today believed that cancerous cells develop daily in the body. The defensive system is strong enough to detect and destroy many of these degenerated cells during the younger years. With increasing age, however, not only does the endogenous defense system become weaker, but, over time, various contaminants also collect in the organism (especially in the fatty tissues). These dangerous substances are said to "accumulate". The damage which is caused to the organism is also seen to be cumulative. The risk increases that these healthy cells may degenerate to form cancer cells. At the same time, such dangerous contaminants as well as a poor psychological state of mind tend to weaken the immunological system. At some point, and here there is a different level applicable for each individual, the limit has been reached. The capabilities of the defensive mechanisms are exhausted and the cancer cells which develop can take advantage of this chance. The risk of developing such a so-called cancer of old age increases.

Included in this group of malignant diseases are pulmonary cancer, breast cancer, stomach and intestinal cancer, as well as cancer of the

Factors	Proportion of deaths due to cancer
Food (nutritional, air and water impurities)	10 – 75%
Tobacco	25 – 40%
Alcohol	2 – 4%
Sexual activity	1 – 13%
Occupation	2 – 8%
Geophysical factors (e.g. sunlight)	2 – 4%
Medications	0.5 – 3%
Industrial chemicals	1 – 2%
Food additives	0.5 – 2%
Infections	1 – ?%
Unknown	?%

Table 6: Causes of cancer development in man (according to R. Doll and R. Peto, J. Nat. Cancer Inst.)

pancreas. In addition, malignant tumors of the male and female genitals, the oral cavity, the pharynx, the larynx, the urinary bladder and the skin also appear more frequently with increasing age. An exception is seen in the malignant diseases of the hematogenic organs, in leukemia and in a number of other cancerous diseases which are frequently observed in children. Apart from the hereditary factors (genetic disposition), virus infections play a primary role in malignant diseases which are independent of age. This relationship has even been verified in individual cases.

Fever is healthy

In earlier times, nearly all individuals suffered from a "common cold" once or twice each year. The nose ran, there was coughing and a fever, while the general feeling of illness tormented those afflicted for a number of days. The patients remained in bed, sweated profusely and usually felt better after a short period of time. This feeling of "malaise" is one of the primary reasons that these people developed cancer substantially less frequently. The episode of a common cold which proceeds intensely is responsible for the elimination of these "sleeping" cancer cells. The fever and the general feeling of illness occurs less as a result of viral or bacterial activity and more as a result of the endogenous defense structures (antibodies, antitoxins and immune bodies). If antibiotics, anti-inflammatory agents and antipyretic (fever reducing) drugs

are already administered at the start of such a common cold, the illness becomes "arrested". Indeed, these agents help to fight the symptoms, but they unfortunately also inhibit the release of substances which serve to destroy the cancerous cells found in the organism. These cancer cells survive and, in the event of a weakened condition of the organism's defense, can reproduce themselves unhindered until a cancerous disease develops. When older people report that they have had no colds with such a feeling of illness for the last three or four years, this can be an indication that their defensive mechanism is too weak. It could be that they are no longer able to react against these bacteria, viruses or even the cancer cells. Dr. Ulrich Abel of the Cancer Research Institute in Heidelberg, Germany proved that cancer is much more prevalent among elderly individuals who, over a longer period of time, had not developed a "real" fever during the course of a common cold. Elderly people who suffer each year from a cold with fever and a feeling of illness which must be cured in bed develop cancer less frequently.

Survival of the tumor cells

Since it has been known that a healthy immunological system is able to destroy tumor cells, discussions have been carried out to discover the mechanisms by which these cancer cells can avoid this destruction. A number of these "tricks" are already known today. These "tumor escape mechanisms" are based on the varied surface structures of the tumor cells so that they are not recognized as being foreign by the immunological defense system and/or as a result of substances which they release to paralyze the immunological cells.

Camouflage with fibrin

The expansive growth (invasive, infiltrative) and the formation of metastases by a tumor are dependent on the coagulatory state of the blood or, stated more simply, on the blood's adhesiveness. Individuals suffering from cancer are more likely to develop thromboses, emboli and venous inflammation (phlebitis). The term "cancer cell stickiness" was already termed very early and could also be demonstrated very easily with the help of very simple experiments. In contrast to healthy cells, cancer cells remain stuck to an inclined glass plate (held at an angle of 45°) after applying them in a watery solution. In fact, the greater the tendency of the tumor to develop metastases, the stronger is the adhesiveness of the cancer cells.

In the course of further research, the idea arose soon afterwards that tumor cells also use the fibrin as a sort of camouflage. They use this

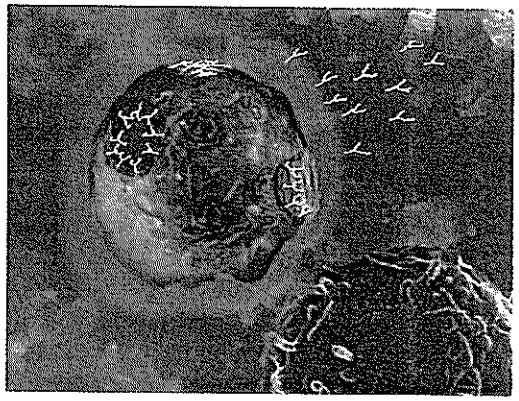

Fig. 44: A tumor cell (middle) demonstrates traitorous antigens (yellow). It makes use of four "escape mechanisms" in order to deceive the immunological cells (lower right). These immune cells are unable to react.
1.The antigens are discarded (shedding) (upper right).
2.The antigens are masked with fibrin (right).
3.The cell membrane is turned inwards with the antigens (left).
4.The antigens bind to one another and thereby alter their appearance (above).

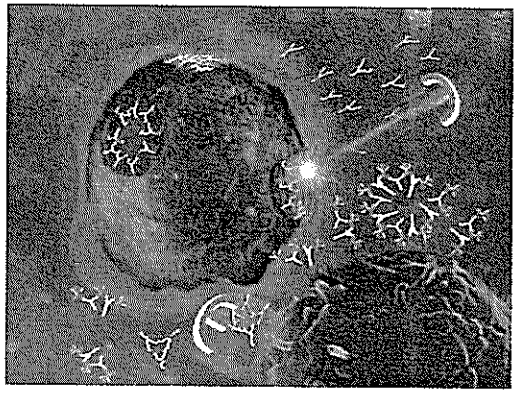

Fig. 45: Enzymes degrade the inhibitory immune complexes (between the immune cells to the lower right and the tumor cell).
Enzymes cause the release of antigens from the tumor cells by eliminating the coating of fibrin.
Enzymes activate the immune cell.

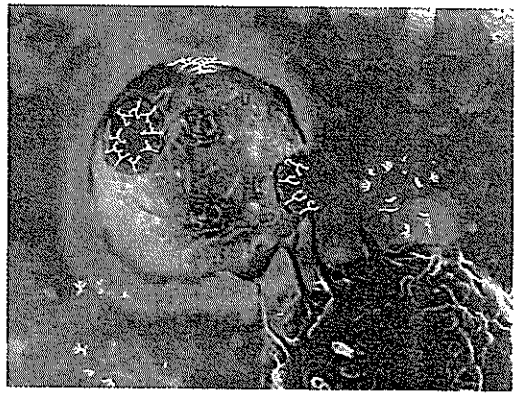

Fig. 46: All factors with an inhibitory influence have been eliminated.
The antigens of the tumor cells are exposed.
The stimulated immune cell now attacks the tumor cell.

fibrin to mask the typical cell-surface landmarks of the cancer cells so that they can no longer be recognized by the immunological defense system. The degradation of fibrin thereby inhibits the development of metastases and also unmasks the typical cell-surface landmarks of the tumor cells for the immunological system. With the aid of hemodiluting agents (anticoagulants), and primarily with the aid of proteolytic enzymes, it is possible to reduce the "cancer cell stickiness" and to inhibit the invasive growth, as well as the development of metastasis which occurs during the course of various cancerous diseases.

Traitorous landmarks of the tumor cells are discarded - (shedding)

A further strategy of the tumor cells for deceiving the defensive system is to shed the traitorous cell-surface molecules. These are antigens which, together with the specific antibodies, build immune complexes. Such tumor cell antigens are also released when cancer cells are destroyed.

Increasing the defensive mechanisms with enzymes – Prophylaxis and therapy

Therapeutic methods which result in an increase in the endogenous defensive capabilities thereby improve the ability of the organism to react with a proper fever and the feeling of illness associated with a common cold. The most important biological treatments of cancer make use of this principle. This is true for all preparations made up of bacterial components, as well as for such substances as found in the lectins of mistletoe and other plant extracts, in Echinacea, vitamin A (compare p. 67 ff.), etc. and in the enzymes.
In the treatment of cancer, such varying enzymes as trypsin, chymotrypsin, bromelain, papain, asparaginase and neuraminidase are used. Every one of these enzymes has proved to be effective against specific types of cancer. Combinations of these enzymes have a substantially superior efficacy.

Immune complexes paralyze the defensive system

If they appear in larger concentrations and have attained a specific size, immune complexes are able to inhibit the immunological cells responsible for the defense against tumors. Researchers recognized these immune complexes as being one of the primary causes for blocking the immunological defense system and therefore called them "blocking factors". Immune complexes in the blood, lymphatic system and tumorous tissue of both men and women play an important role in the development of many types of cancer. This has been investigated rather extensively, primarily for Hodgkin's and non-Hodgkin's lymphomas, reticulosis, hemoblastosis, carcinomas of the chest, lung and stomach, as well as in a series of studies performed on patients suffering from colon, pancreas and ovarial carcinomas or on individuals with melanomas.

A number of technological procedures are available for eliminating immune complexes from the blood stream (plasmapheresis, lymphocytapheresis, cryoprecipitation, infusions with protein A). In the US, the technological possibilities of immune complex elimination (compare also p. 112) have already been applied successfully for a few malignant tumors. In various studies, it has been shown that systemic enzyme therapy causes a degradation of the immune complexes and supports their breakdown through the promotion of phagocytosis.

Defensive cells against cancer (compare p. 36 ff.)

A number of defensive systems are available to the organism for the direct attack and destruction of cancerous and virus-infected cells.

Stimulation of the natural killer cells and the macrophages

One of these defensive systems consists of the macrophages and the natural killer cells. These cells are able to track down virus-infected degenerated cells in the organism and subsequently drill actual holes in their cell membrane. In cancer patients, however, the cancerous cells have been able to substantially reduce the aggressiveness and the effects of these cells of the defensive system.
Proteolytic enzymes which are able to switch off various "escape mechanisms" of the cancerous cells have a direct stimulatory effect on the macrophages and the NK cells. The tumoricidal feature of these defensive cells increases twelve-fold to that of the initial value. This stimulation brought about by enzyme therapy will most certainly lead to favorable results in the treatment of various types of cancer.

Cytoclastic lymphocytes

The so-called T lymphocytes also play a very important role in the endogenous defense system against cancer. These T lymphocytes are also able to recognize and destroy the cancer cells as well. One portion of these lymphocytes, the cytotoxic (or cell poisoning) lymphocytes,

attack the tumor cells directly. Like the macrophages and the NK cells, they can penetrate into the tissues of the tumor, identify the cancer cells by way of their surface molecules and finally destroy them while in direct contact.

Cell-messenger substances as a weapon

The defensive cells which have been described can also destroy cells infected with viruses and degenerated cells which are in direct, cell-to-cell contact. In addition, there is a sort of "long-range weapon" which is active against the tumor cells as well. Primarily the macrophages make use of this additional tool. More than 20 years ago a substance was isolated from specific immunological cells which was even able to destroy cancer cells and virus-infected cells. Today, this cell messenger substance called tumor necrosis factor (TNF) is known to be a relatively small molecule, although it has attained great importance in both science and research.

If the organism concentrates its energy toward the elimination of the cause of a disease, the secreted tumor necrosis factor (TNF) which functions along with the other cytokines plays an important role. Inflammatory substances (mediators) are released, and the fever as well as a feeling of being ill develop. What is especially important, however, is that the cancer cells existent within the organism can actually be destroyed by the liberated TNF. Cells which are infected by viruses are also destroyed on this occasion. The activated phagocytes are then occupied with the removal of the cell fragments which remain. These fragments are engulfed and then broken down.

Benign and malignant TNF

Unfortunately, TNF is only effective against cancer cells to a certain degree. Should the TNF molecules unite to form large structures (polymers), or should they become bonded to receptors which have been discarded (that is, "shed") from the tumor cells, they lose their carcinolytic capabilities. Nevertheless, these TNF molecules remain responsible as a trigger for the feeling of being extremely ill. A disturbance in the TNF balance, the TNF production and the TNF secretion is primarily observed in the later stages of chronic (autoimmunologically-derived) or malignant diseases during which the physiological equilibrium of the immunological system can hardly be maintained.

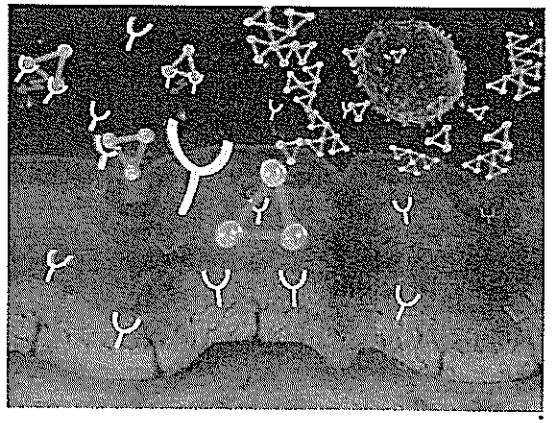

Fig. 47: The triangular TNF molecule (blue) normally binds to specific receptors (yellow) of the tumor cell membrane and then destroys the tumor cell. When too many TNF molecules are formed (triangles), they bind together to develop monstrous molecules. In this way, they lose their carcinolytic effects and nevertheless cause a weakening of the patient. The tumor cells then discard these TNF receptors (yellow) in a process known as shedding. Triangular TNF molecules which remain active are thereby captured. The immune cells (upper right) are blocked by the numerous molecular complexes.

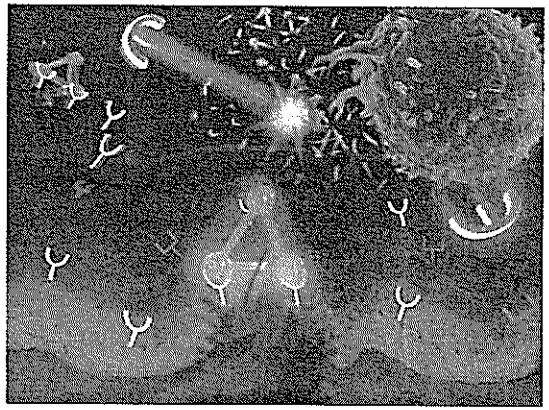

Fig. 48: Enzymes destroy the monstrous TNF molecules and the triangular TNF molecules which are bonded to captured receptors. The blockage of the immune cell is thereby suspended. Enzymes stimulate the immune cells to attack. A triangular TNF molecule binds to TNF receptors (yellow) on the cell membrane and destroys the tumor cell.

Enzymes can bring about an improvement in the massive general manifestations of the illness from which so many severely ill patients so frequently suffer. It has only recently been determined how this functions. The enzymes are bonded to transport molecules in the blood stream. The most important transport molecule is the α_2-macroglobulin, a substance which is also partially responsible for regulating the effects of the

TNF. By way of this interreaction with the α_2-macroglobulin, proteolytic enzymes can also have a regulatory effect on the disturbed metabolism of cell messenger substances.

Furthermore, proteolytic enzymes break down the bonds of TNF molecules with the inhibitory, "shedded" receptors, as well as with the TNF polymers. The TNF is thereby converted to its original carcinolytic form once again.

Clearly, all three of these mechanisms play a part in the positive influence of systemic enzyme therapy on the treatment of cancer. These recent discoveries are expected to play an important role in the development of newer therapeutic strategies for the treatment of cancer.

Secondary prophylaxis – Avoidance of recurrencies and metastases

Enzyme therapy reduces the risk of cancer recurrency following a successful treatment with surgery, radiotherapy or chemotherapy. Should no evidence of a malignant process be observed during the first year after a successful initial treatment, an interval therapy with the use of enzyme combination preparations can be carried out. Professor Ottokar Rokitansky, a well-known Austrian surgeon, has collected a wealth of information in the long-term therapy of patients with breast cancer. In order to appreciably reduce the risk of recurrency and of metastasis, and following a successful maintenance therapy with enzymes, he recommends the subsequent use of an interval therapy with enzymes for the following three years.

Enzymatic alterations of special adhesive molecules and the inhibition of metastasis

Most cancer patients do not die as a result of the primary tumor, but rather as a consequence of the subsequent metastases. In order for metastases to develop, cancer cells from the tumorous growth must pass into the circulatory system via the blood or lymph tracts. These cells then adhere to other sites within the organism, for example on the inner walls of the vessels. From here, they penetrate into the surrounding tissues, multiply and ultimately form a metastasis. It has long been known that the "adhesiveness" of the blood and of cells is increased during chronic and malignant disease. The excessive development of fibrin has been made responsible for this phenomenon and for the "adhesion" of the cancer cells.

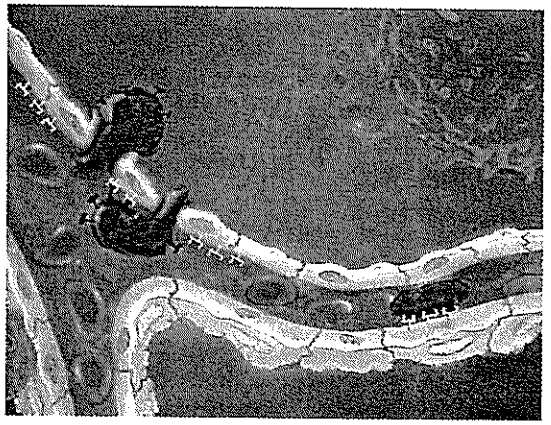

Fig. 49: By way of special adhesion molecules (black) such as vitronectin or CD44, the tumor cell is able to adhere to the inner wall of a vessel. The endothelial cell withdraws, the tumor cell can penetrate deeper into the surrounding tissue (infiltration) and eventually develop into a metastasis. A macrophage of the tissue is seen in the upper right of the illustration.

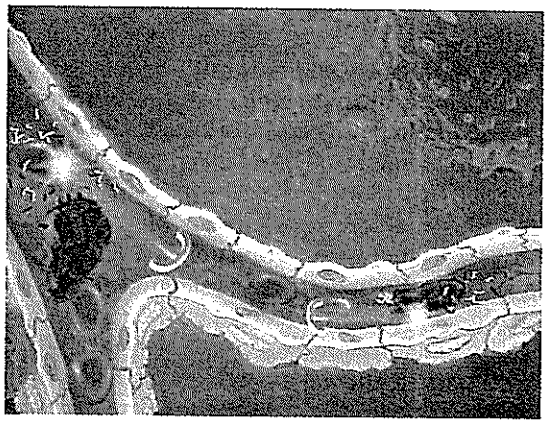

Fig. 50: Enzymes alter or hinder the development of the receptors responsible for metastasis. In this way, it is impossible for the tumor cell to bind to the vascular endothelium. The development of metastases is thereby hindered or at least inhibited.

Recently, evidence has been found that the metastasis of certain cancer cells also requires other agents. In order to adhere to the inner wall of vessels (endothelium), they make use of special agents, the so-called adhesion molecules, which are found on the cell surfaces. These cancer cells are only able to penetrate into the tissue (infiltration), to grow and to eventually form metastases after having established contact with an endothelial cell via these adhesion molecules. In the development of the malignant melanoma, for instance, the adhesion molecule vitronectin is of essential importance.

Dr. Lucia Desser of the Institute for Tumor Research and Tumor Development of the University of Vienna, Austria was able to prove that enzymes hinder this adhesion by preventing the formation of vitronectin on the cell surfaces. The enzymes are thereby able to inhibit the development of metastases. Similar relationships were also seen for the metastasis of breast and colon cancer. Here, a different cell-surface molecule, the CD44 receptor, is held to be responsible for metastasis. Dr. Rudolf Kunze of Berlin, Germany demonstrated that proteolytic enzymes are able to alter this adhesion molecule to such an extent that the formation of metastases can be inhibited. These findings provide an explanation for the effects of enzymes in the prophylaxis of metastasis which have already been observed for more than 30 years.

Chemotherapy and radiotherapy is improved through the concomitant application of enzymes

Apart from its use in the primary and secondary prophylaxis of metastasis, the application of systemic enzyme therapy accompanied with chemotherapy and/or radiotherapy has proved to be very important for the treatment of cancer. Enzymatic preparations have also proved to be effective in concepts of adjuvant therapy. Dr. Schedler of the Department of ENT of the University of the Saar in Homburg, Germany has demonstrated that enzyme combination preparations can help to reduce the adverse effects frequently associated with various chemotherapeutic agents. The chemotherapy is more effective and is tolerated better by the patient since the adverse effects are much milder. The internationally renowned oncologist Professor Sakalova of Prague, Czechia Republic has reported similar success in the treatment of patients with multiple myelomas. If additional enzyme therapy is given concomitantly to the chemotherapeutic regimen, remission of the disease is more rapid and the patients suffer less from the adverse effects of the aggressive cytostatic agents. The time until recurrency of the disease was observed could also be prolonged with this additional enzyme therapy. At the same time, the pathological laboratory findings (especially those of the important paraproteins associated with this type of malignant disease) were seen to be appreciably better in this group than in comparative groups treated with the conventional chemotherapy alone. According to present knowledge, the success thereby obtained can be recognized as a method for achieving a prolongation of life.

Proteolytic enzymes are also seen to offer protection against the adverse effects of a radiotherapy, a method of treatment with which certain types of cancer can be treated quite successfully. Radiotoxemia (radiation sickness), a feeling of malaise with a relatively long-term reduction in the endogenous defensive powers, is a side effect which is seen most commonly following radiation therapy. In a large-scale clinical investigation performed by Professor Beaufort of the University of Graz, Austria, the concomitant application of enzyme combination preparations together with a radiotherapy could be documented as being able to provide a substantial reduction in the adverse effects. The patients were therefore able to tolerate the therapy much better. This protective effect of proteolytic enzymes could also be seen in the reduced symptoms (inflammation of the mucous membranes) following radiation therapy which has been carried out in the region of the mouth. The progress of a radiogenic mucositis can clearly be influenced positively through the use of an enzyme therapy.

Prophylaxis of lymphedema

Surgical procedures and radiotherapy which also involve the lymphatic tract frequently result in severe lymphatic blockage and lymphedema of an extremity. An example for this which is often observed is the lymphedema of the arm following breast surgery as a treatment of breast cancer. As demonstrated in clinical studies, systemic enzyme therapy is able to hinder the development of such complications or can at least substantially reduce their severity.

Mastopathy

Palpable nodes and nodular alterations of the glandular tissue in the breast are, of course, seen to be disturbing findings. The women who consult their physicians with such complications are frequently seen to be quite young as well. The therapy often ends with a visit to a surgeon who must remove this node. Although a number of physicians recognize this mastopathy as being a preliminary stage to a cancerous disease, these frequently painful alterations of the mammary glands are actually benign. The fine-tissue, microscopic investigations reveal that the superficial cells of the mammary ducts (endothelium) demonstrate varying intensities of growth. As is frequently the case, the cause of this disturbance involving the entire breast is unfortunately unclear.

Thus far, medicine has only been able to do little for the women afflicted with this illness since no sufficiently reliable and effective therapy has been available. From earlier experimentation performed on ani-

mals, Dr. Wolfgang Scheef of the Robert-Janker Clinic in Bonn, Germany was aware that a combined therapy of proteolytic enzymes and vitamin E leads to a recession of benign tissues of the connective tissues (fibromas) and even to a recession of breast cancer. An attempt to treat mastopathy with enzymes and vitamin E therefore seemed to be well grounded. The success was astounding. After only six weeks, 85% of the patients had no complaints after undergoing such a treatment. Many of them even demonstrated a complete remission of the nodular alterations. Recently, Professor Dittmar of a teaching hospital in Starnberg, Germany completed a large investigation which included a total of 96 patients from numerous clinics. Through the systemic enzyme therapy, the symptoms of pain, a feeling of tenseness, as well as the swelling of the breast, improved substantially. The physicians documented the therapeutic success with the aid of objective ultrasonic investigations. They were able to prove that the nodular and cystic alterations of the breast tissue had indeed regressed. The additional administration of vitamin E (500 IU to 1,000 IU) and vitamin A (10,000 IU) improved the results of the systemic enzyme therapy even further.
The "fibrocystic mastopathy" is a common illness, approximately half of all women are afflicted. Naturally, it is important that the preventive medical examinations not be neglected. Nevertheless, a therapeutic attempt with the risk-free application of a proteolytic enzyme combination preparation and vitamin E is certainly worthwhile. Generally, the illness can thereby be treated successfully within a matter of only a few weeks. Even patients who have demonstrated such tissue changes over a number of years are frequently influenced positively after a mere six weeks.

Summary

At a time when it was first possible to perform more exact investigations of living processes, those skilled in the medical sciences considered the human organism to be a functional unit. Correspondingly, therapeutic attempts were carried out taking this into account. Here, special consideration was given to the general detoxification of the body from waste products and contaminants, the accumulation of which has been held responsible for many diseases.

Advancements in medicine have increasingly placed the organ-specific considerations in the foreground, whereas the idea of a total system involving a reciprocal influence and mutually dependent organ relationships has simply been forgotten. Every illness, even if it initially only affects a single organ, ultimately affects the entire organism to a greater or lesser degree. This may occur directly through the lack of a specific metabolic product (organ failure) or indirectly by way of feedback mechanisms (nervous stimuli, psyche and metabolism). The discovery that the cells of the immunological and nervous systems communicate directly with one another via cell messenger substances and receptors has led to the establishment of the new science of psychoneuroimmunology.

Although there is presently no doubt as to the importance of the immunological system in maintaining the condition of health, science is today only at the beginning of truly discovering the importance of the immunological system. The immunological system in humans makes use of resources which enable a constant adaptation to the changing environmental conditions. Nevertheless, these resources are not inexhaustible. Apart from the constantly increasing environmental burdens, modern woman/mankind is also exposed to ever increasing psychological tensions whose importance for health are only gradually being recognized. In the development of chronic and malignant diseases, these relationships are especially important and they must be taken into consideration increasingly when contemplating therapeutic possibilities. Today, in many hospitals and in the clinical institutions of numerous universities throughout the world, intensive efforts are being made to develop therapeutic strategies which take into account the assistance that can be provided by the immunological system. Not only the immune activation, but even more the immunoregulation, stands at the forefront of these efforts.

Proteolytic enzyme combination therapy plays an important role in these holistic therapeutic approaches. Their effects for the most varied of indications have been verified in numerous clinical investigations. More recent knowledge of immunology helps us to better understand the possible mechanisms of enzyme effects. In the event of such acute health disturbances as infections and injuries, the application of proteolytic, enzyme combination preparations is important for two different reasons. On the one hand, they support the immunological system. On the other, excessive reactions are reduced so that the possible chronification of damage is opposed. Proteolytic enzymes also support various aspects of the defensive system. They more or less increase the natural resources of the immunological system and thereby have a regulatory effect on the immunological state of equilibrium. The chances of treating a chronic illness or a cancerous disease successfully are thereby improved substantially as well. Especially in the treatment of cancer, enzymes unfold effects which are directed explicitly against the tumor cells. Proteolytic enzyme combinations prove to be worthy in all phases of chronic and malignant diseases both in a form of therapy which makes use of a combination with other measures as well as in a monotherapy.

Enzymes are not the only immunoactive substances (for example, consider also thymus gland peptides, mistletoe lectins, interferon, interleukin, vitamin A, etc.) which belong to the class of "biological response modifiers" (BRMs). The diversity of life, however, offers a number of problems for human medicine. A therapeutic strategy which may be used successfully to treat a patient with rheumatism or a tumor may be useless in the treatment of a different patient with the same disease. Too little is known about the immunological defense mechanism and its regulatory functions. It could be possible that the immunological system does not attack tumor cells intentionally since they have a structure similar to that of other healthy cells in the organism and therefore cannot be destroyed selectively. Initially, the immunological system selects the lesser evil, it tolerates the growing tumor in order to avoid the immediate destruction of a vital organ. In the sense of evolution, this gain in time provides a possibility for reproduction.

The sensible and flexible combination of various BRMs with an established, organ-specific therapy offers a new and hopeful approach for holistic therapy. This holistic therapy, however, is still at the beginning of its development.

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