### Forschungsinstitut zur Traditionellen und Modernen Europäischen Medizin



## On the current significance of salutognesis

Natural science has been shaping our medicine for more than 300 years. With numerous objectifying procedures of counting, weighing and measuring, the human body is examined down to its biological, molecular-biological and genetic processes.

More and more research and analysis is carried out to find further regularities, causal relationships, mechanisms of action and protective factors. This approach has perfected human medicine in many ways, very successful and effective, especially in acute and life-threatening diseases.

In the 19th century, after the discovery of the anthrax bacillus and the tubercle bacillus by Robert Koch, infectious diseases became not only successfully treatable by antibiotics, but also preventable by prophylaxis and hygienic measures. A new way of thinking set in in medicine and the infection model was launched. It became accepted that everything that caused illness came from outside, scientifically justified.

This way of thinking and acting was probably true for bacteria and viruses, but was also transferred to bio-social and economic-political conditions. The sufferer himself was only granted a passive role in the disease process and understanding. Since everything that caused illness came from outside according to the prevailing scientific logic, it was determined that everything that healed must also come from outside. This attitude was the accepted logic and reflects the modern welfare state with the ever-increasing industrialisation and globalisation of the economy.

As a result of this development, people in the developed industrialised countries were increasingly detached from their social-family milieu and from rural relationships as well as grown structures and contexts. The consequence was that more and more help was sought from outside, from the anonymous solidarity community.

The more the welfare state institutions became helpful, the more the individual with his or her individually and subjectively determined demands and needs lost significance. The established, generalised social system was mandated by the legislator to provide for the population according to established objective guidelines and, of course, to determine what was generally good and right and appropriate for the individual.

With great effort, medical research now devoted itself to the so-called risk factors, which were held essentially responsible for the development of diseases. All in all, the question of everything that makes people ill was in the foreground of thinking!

But what actually is health? We are all familiar with the much-cited WHO definition. However, health as a unity of physical, mental and social well-being also makes it clear to us that the transitions from health to illness are fluid.

The definition of health prevents it from being seen only as the absence of visible or testable diseases, e.g. a broken limb, an abnormal blood count, a cancer. Health means more than not having a cold.

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Health is closely and inseparably linked to the individual and also starts with the individual himself. It is up to the individual to determine and decide whether he or she feels healthy or ill. And so the concept of health and illness will show intra-individual as well as geocultural and political differences.

For example, in the case of man's first protective reflex, fear, we know of sky-wide differences between the peoples of Europe and Asia. The same applies to pain as a symptom of illness, which is also processed differently within the various cultures. The Indians of North America can withstand relatively severe pain without any effort and have their own evaluation for it. The situation is completely different for Western Europeans in terms of how they process pain.

In the future, medicine will have to work out strategies, first of all for dealing with the disease and secondly for dealing with circumstances that can negatively influence our physical, mental and social well-being. After that, these strategies must be communicated to people and trained on how to deal with them.

A large part of the future of health lies in the individual himself, in the individual's own responsibility for himself. We humans bear responsibility everywhere: parents are liable for their children, employees for the work they have done, politicians for their policies, doctors for their actions, but no one wants to take responsibility for their own health. Individual responsibility can be limited and must be clearly defined by health authorities. In cases where the individual can no longer bear this responsibility, the solidarity-based health system must help to maintain health or treat diseases.

Global economic development and its effects on medicine will force us, if only for reasons of cost, to demand that people take responsibility for their own health. As doctors, we must encourage our patients to rethink, so that they actually do what they can themselves to maintain their health and do not rely solely on treatment with medicines and operations.

We doctors, too, have to change our way of thinking, because we, too, have been trained not to believe primarily in the patient's self-healing powers and personal responsibility, but above all in medical action with an immediate effect. A completely different way of thinking emerged in the last quarter of the 20th century, when some scientists asked the question: "Why do people stay healthy?", e.g. when there is a wave of influenza, no one is surprised that suddenly many people fall ill, because thinking in terms of the infection model prevails.

But the question arises: Why are certain people always able to stay healthy, despite the same health-damaging influences with which they are also confronted? How do people manage to get back up from life-threatening illnesses on their own? What kind of people are they who do not become ill despite extreme stress? As a logical conclusion, attempts have been made not only to study how diseases develop, but also to analyse how health develops and why it persists. The German researcher Virchow had such thoughts and shared them with his colleagues at the Natural Scientists' Meeting in Insbruck in 1869.

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He referred to the assessment of regulation for determining the boundary between health and disease. His Russian colleague Pavlov saw health as a dynamic equilibrium between organism and environment, and disease as a disturbance of this equilibrium.

According to Pavlenko (1973), Hecht and Baumann (1974): A definition of health makes it necessary to include sanogenesis in the medical practitioner's way of thinking in addition to pathogenesis. According to Hecht and Baumann, sanogenesis is understood to be a functional complex of protective and adaptive mechanisms that are mobilised in the dynamic organism-environment relationships depending on the prevailing stimulusresponse constellations in each case, with the aim of maintaining the optimisation of the regulatory processes in the organism or restoring them in the event of disturbances.

Sanogenetic and pathogenetic processes are in a regulatory equilibrium with each other; if salogenesis predominates, health is present; if pathogenesis predominates, then the first pathological processes develop. This principle forces us physicians to investigate how diseases develop and, analogously, how health can be maintained or why people become healthy again after overcoming illnesses. We take the view that health cannot be regarded as a normal state.

The healthy person is therefore constantly between the poles of perfect health and perfect illness. This means that the human being should not only wait with fear for disease-causing risks, but also conversely learn to live in harmony with disease-causing risks and burdens as far as possible and to use these factors to intensify our life processes. This attitude develops and strengthens self-confidence and leads to an expanded knowledge of illness and health.

It is well known that a serious illness in one's own body changes the relationship to our surroundings, to the environment, to nature and to the ever-recurring act of creation. New experiences occur and the affected person sees life and its determining factors from a different perspective and lives the remaining existence more in his physical inner being and more intensely in his soul as well as more consciously with his mind / spirit.

For the coming centuries, it will be an urgent task for us doctors to convince patients of a salutogenetic concept in order to avoid spending billions in health care for the apparent maintenance of human health. There are whole branches of industry that exist only to sell the most miraculous medicines or devices to apparently healthy people who complain of more or less harmless complaints. The profits made from this, in the tens of billions of euros, could then be invested more sensibly in the actual maintenance of health or in the prevention of future serious diseases or epidemics, in prophylactic medicine.

With the discovery of the phenomenon of photoreactivation in bacteria by Albert Kellner in 1949, based on the repair effect of a photolyase stimulated by visible light, a number of enzymes were discovered that participate in DNA repair. This means primarily the removal of primary DNA damage or correction of secondary damage and secondarily tolerance of DNA damage.

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Some repair mechanisms are of enormous importance for the concept of salutogenetic medicine. Of the multitude of different damages to DNA induced by alkylating agents, one lesion has emerged as particularly important: alkylation in the O6 position of guaninine. If not repaired, it leads to OC-AT type base mismatches.

This minor lesion is the main culprit for the induction of malignant cell transformation after exposure to alkylating carcinogens, such as the methylating N-nitrose compounds. The repair capacity of cells and tissues depends on the amount of their alkyltransferase and the speed of the new synthesis of the protein, e.g. human liver cells contain many molecules per hepatocyte (approx. 100,000), whereas the brain contains less alkyltransferase (10,000 molecules). This importance of the repair protein in the protective system of the cells against carcinogenic exposures and thus for maintaining the health of the organism has already been impressively demonstrated in genetically manipulated cells and transgenic animals.

Furthermore, it could be shown that cells without alkyltransferase are considerably more sensitive to the cytotoxic, mutogenic, recombinogenic and chromosome breakage-induced effects of alkylants than alkyltransferase-positive cells. The protective effect increases with increasing concentration of alkyltransferase. Alkyltransferase plays an important role in the prevention of genotoxic effects and counteracts the development of cancer after exposure to alkylants.

The opposite conclusion is that a reduction in MGMI repair capacity increases the risk of mutagenesis and can thus lead to the development of metabolic diseases and cancer. This fact is closely related to the three salutogenetic properties of alkyltransferase:

- 1. alkyltransferase also protects cells from the toxic effects of cytostatic drugs that have a methylating or chloroethylating effect. It is an important determinant of the resistance of tumour cells to drugs (dacarbazine, procarbacin, streptozotocin, etc.)
- 2. Alkyltransferase can be selectively or almost completely blocked by inhibitors without toxic side effects.
- 3. The alkyltransferase concentration increases in some tissue types after exposure to genotoxic stress factors (X-rays, chemical mutagens and carcinogens) and glucocorticoid hormones, and the gene is inducible.

From these experimental findings, a number of salutogenetic conclusions and possibilities can be derived with practical application, which are aimed at recovery and maintenance of health:

Measures: To avoid the formation of alkylation damage

- Avoidance of endogenous formation and intake of nitrosamines, e.g. balanced whole foods and efficient acid-base balance, the administration of vitamin C

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- Recognition of exogenous and endogenous factors that inhibit DNA repair by alkyltransferase, e.g. critical exposure to formaldehyde and heavy metals at work and in the home
- Recognition of people with low alkyltransferase repair activity as a risk group, as they are at extreme risk of being damaged by the carcinogenic effect of alkylating substances, e.g. nitrosamines in food and luxury foods as well as cigarette smoke, the rubber industry and other environmental toxins. Here, salutogenetic cards for people with low alkyltransferase concentrations in the blood cells should be considered, in order to show people in a state of repair with informative information and to build up health-oriented behaviour based on this
- The protective effect of alkyltransferase reveals salutogenetic applications in tumour therapy, e.g. by determining the expression of the repair protein in tumours, the prospective resistance of a cancer and thus the curative response can be predicted after administration of methylating and chlorethylating cytostatic drugs. By selectively inhibiting alkyltransferase in cancer tissue, tumour sensitisation and thus a significant improvement in cytostatic efficacy can be achieved by adjuvant administration of O 6-benzylguanine or O 6-alkylguanine derivatives that enable targeting

Again, transfer of the alkyltransferase gene in healthy tissue could protect against chemotherapy, avoid or reduce acute toxic side effects of therapy, such as haematopoietic depression, lung failure. Furthermore, the undesired therapy-related secondary tumour formation could also be reduced.

DNA alkylation damage and also the oxidative DNA damage as well as other base modifications with genotoxic effects are removed by base excision. Several enzymes are involved in this process.

The key enzymes are glycosylases, which recognise specific base damage and remove it from the DNA. The damage that is not recognised by damage-specific glycosylases and causes deformation in the DNA and a transcription and replication block is repaired by nucleotide excision.

This repair takes place in two ways:

- 1. The repair of active genes
- 2. The repair of inactive genes

Screening to identify heterozygous repair-deficient individuals can be considered a preventive salutogenetic measure. The knowledge of the importance of DNA damage, especially oxidative DNA damage induced by light exposure - UVA/B, should lead to targeted health-conscious behaviour and preventive measures should be demanded.

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Such as avoiding excessive sun exposure or use of sunbeds, the choice of appropriate clothing and cosmetics, e.g. the use of skin protection products with antioxidants and sun protection factors. In the future, it will be possible to use repair enzymes (photolyase) in skin protection products to enable targeted repair of DNA in the cells of the skin after sun exposure.

Strategies for the transfer of nucleotide and crosslink repair genes are currently being tested in order to correct the repair defect in Fanconi anaemia and thus to build up protection against the development of blood cancer in this form of anaemia in the sense of salutogenesis.

Another possible application in the sense of strengthening people's natural self-healing powers is the transfer of repair genes to protect the tissue in healthy cells before and during high-dose chemotherapy. The doctor of the future will have at his disposal an arsenal of genes and repair genes that have a detoxifying effect and bring about drug resistance by inhibiting apoptosis. In this way, it would be possible to optimally and meaningfully supplement a cytostatic drug used by reducing its systemic toxicity and, in the long term, possible secondary tumour formation or side effects. This will make it possible in the future to use very targeted strategies to strengthen the body's own defences.

Some other DNA damage can lead to base mismatches, as well as base exchange mutations. One of the strongest causes of base exchange mutations is oxidative stress or consequences of irradiation that induce 8-oxy-guanine. If this damage is not repaired pre-replicatively, the cell switches on a downstream repair system, which then removes bases that have been incorrectly incorporated into the DNA. The repair system has a monitor that allows the enzymes to distinguish between daughter and parent strands. Mismatch repair relies on the concentrated action of several enzymes and is also controlled by several genes. Mutations in these genes lead to genomic instability and the affected genes, which regulate cell proliferation, cannot fulfil their function. This can lead to malignancies, such as hereditary non-polyposis colon cancer.

Induction of repair genes results in increased repair of O 6 - alkylguaninine by providing an increased amount of alkyltransferase per cell, and thus better survival and a reduction in the frequency of the mutation.

The pathogenetic principle of the development of diseases that have a genetic disposition is based on the thesis that endogenous and exogenous noxae cause DNA damage that can lead to mutations, which in turn can lead to many metabolic disorders, autoimmune diseases, ageing and cancer. The human organism is not exposed to this fatal sequence of conditions without protection. Protective mechanisms are at work to protect the cells from DNA damage.

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DNA repair, through which the initial state in the DNA can be restored, is of outstanding importance. DNA repair is a process aimed at maintaining the health of the cell and the entire organism, which has great salutogenetic significance. Another process that is important from the point of view of salutogenesis is apoptosis. These two processes, repair and the programmed death of very severely damaged cells that can no longer be repaired, counteract pathogenesis and represent self-healing forces of the organism that have slowly been uncovered in their complexity. This also concerns the inducible cellular mechanisms with a protective function, furthermore also the cell cycle - regulating factors - as well as the repair proteins.

Through a better understanding of these processes, it will be possible to exert a targeted influence on them with the aim of activating the cellular protection system against genetic disorders as needed, depending on the influence of disruptive factors from natural, partly selfgenerated stress situations (e.g. psychological stress, sunbathing) or in the case of a necessary use of tumour therapeutics. DNA repair is a vital, irreplaceable process for the human organism.

DNA repair processes are an impressive example of the organism's self-healing powers and possibilities. The practical consequence of a salutogenetic treatment concept is first and foremost to support and maintain these, oriented towards molecular biological and biophysical findings. Secondarily, salutogenetic therapy principles should have other goals in the concept with DNA - repair. Salutogenetic measures should also be directed towards preventing DNA damage in the sense of prophylaxis in the sense of monitoring DNA repair defects and, through their detection, recognising people predisposed to genetically determined diseases. To eliminate influences that inhibit protective functions and to stimulate DNA repair, especially in stress situations such as tumour therapy, for example through adjuvant therapy measures.

In the future, it will be possible to strengthen the body's self-healing powers by transferring DNA repair genes into cells with a low repair capacity of otherwise healthy people and to better withstand tumourigenic exposures in the sense of curative prophylaxis.

In the sense of salutogenesis, we can also define self-regulation according to Pavlov and Grossarth-Maticek, as a person's ability to create conditions that lead to or maintain wellbeing and inner balance, i.e. health, through their own activities. Through numerous studies it could be recognised that the degree of self-regulation essentially determines the course and prognosis of diseases.

Thus, we had to realise that the question "What makes us ill?" without taking the individual into account can only be answered from knowledge of general and pathogenetic laws, and can also only be answered inadequately. The next question, however, "Why does a person stay healthy?" requires an answer that can only be answered from knowledge of the specificity of the individual person.

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By posing and dealing with these questions, a development has come into medicine that pleasantly complements the long-held approach of pathogenesis. The question of what makes people ill has launched care medicine. The question of health and health maintenance has developed an individual, self-responsible medicine.

The health care system of our age essentially needs the synthesis of these two approaches.

I understand salutogenesis as the first theoretical and practical medicine that corresponds to the globalisation of our time and unites on the one hand the natural scientific approach and on the other hand the spiritual scientific approach in the sense of holistic medicine of body, soul and spirit. Furthermore, salutogenesis also leaves room for the use of knowledge and experience from the medicine of the most diverse cultures of the peoples of our civilisation.

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