NADH:

The Biological Hydrogen

The Secret of Our Life Energy

- Hydrogen—The New Energy Supplement
- A Potent Antioxidant & Immune Enhancer
- Therapeutic for Parkinson's Disease, Chronic Fatigue, Alzheimer's Dementia, and Other Conditions
- Boosts Athletic Performance & Longevity
- Safe, Effective, & Natural

George D. Birkmayer, M.D., Ph.D.

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This book is dedicated to my wife, Karin,
and my children Florian, Sophie, Heidi,
Benjamin, Ferdinand, and Carina,
the joy and spirit of my life,
in appreciation of their
love and affection.

Preface

If you could take a natural substance that occurs in every single cell to increase your overall energy, would you?

If you could take a natural substance that boosts the immune system and protects your cells from damage, would you?

If you could take a natural substance that enhances your cognitive capability and improves your memory, would you?

Most people would answer, “Of course.” This book will inform you about this substance, what it is, what its biological functions are, and how this substance improves physical and mental performance in healthy individuals and helps with ailments caused by an energy deficiency.

The biological form of hydrogen occurring in our body reacts with the oxygen present in every living cell to produce essential energy. Most people get a sufficient supply of oxygen for energy production from the air they breathe. The limiting factor in our body is hydrogen—hydrogen is absolutely necessary for the energy production in our cells. Thus, the biological form of hydrogen is the secret of our life energy.

This book will inform you about NADH, the biological hydrogen, its functions that are essential for life, and its multiple effects in the human body.

CHAPTER 1

What Is NADH?

The most promising natural substance in our body is NADH, which stands for nicotinamide adenine dinucleotide hydride. NADH is the biological form of hydrogen. It reacts with the oxygen present in every living cell, thus producing energy and water. The more NADH a cell has available, the more energy it can produce, the better it functions, and the longer the cell (and the entire organism) lives.

Is it possible to increase the amount of NADH in the cell by adding NADH from outside? The answer is: yes. This implies that we can increase the energy level in our cells. Due to this, the cells can produce more of all the components essential for life, and thus they will function better and live longer. This is feasible by supplementation with NADH in order to boost the hydrogen taken up by the human body.

The amount of NADH a cell contains depends on the amount of energy it requires. The heart and the brain need the most energy of all our organs. Hence, these organs benefit the most from an external supply of NADH. All other organs, particularly the lungs, the liver, and the kidneys, also get more energy from NADH and function better. The biological hydrogen is the fuel for cellular energy production, and nutritional supplementation can provide our body with more NADH.

THE BIOLOGICAL HYDROGEN

The *H* in NADH stands for hydrogen. Pure hydrogen is highly reactive: if you throw metallic sodium into water, hydrogen is formed in a tenth of a second. The reaction forms so much heat that the hydrogen ignites instantly. If the hydrogen would react like this in living cells, they would explode. The hydrogen in NADH is the biological form, as it is bound to the molecule NAD in the cell. Due to this, it does not react in an explosive-like manner. Hydrogen must be inserted into a molecule in which it is not as reactive as in its pure form. Nature has solved this problem by forming the molecule nicotinamide adenine dinucleotide hydride, or NADH.

Though the hydrogen is still very reactive in this compound, it does not inflame spontaneously. Yet it does react with the oxygen in the cell in a cascade-like biochemical reaction forming water and energy. This happens in every living cell. Hydrogen and oxygen are thus the most important elements for energy production in our cells. In fact, biological hydrogen is the secret of our life energy.

Nicotinamide, which is also part of the NADH molecule, is also known as vitamin B_3. Nicotinamide is produced in the body, is a natural biological substance, and is biochemically the precursor of NADH.

NADH HAS BEEN KNOWN FOR 100 YEARS

NADH was discovered in 1903 as a co-factor for the fermentation of alcohol by yeast. Since then, it has been found that this coenzyme catalyses more than a thousand metabolic reactions in the body.[1] NADH is the most important of all coenzymes discovered in the human organism; hence, it carries the name coenzyme-1.

A coenzyme is a substance essential for enzymes to gain full functionality. Enzymes are large biological molecules that catalyze many biochemical processes necessary for our organism to function properly. They lead to products needed for full vitality of cells and organs. Enzymes can be compared to production machinery in a factory that transposes one material into another one. In living cells, enzymes catalyze the breakdown and turnover of the carbohydrates, lipids (fats), and proteins we take up with our daily food into smaller units. These small units are further metabolized and a large part of them are converted into NADH.

For more than fifty years NADH has been used in its pure form in laboratory tests to determine metabolic glucose, uric acid, or cholesterol levels in the blood. Pure NADH is isolated from yeast. Yeast contains relatively high amounts of NAD, the oxidized form of NADH. Yeast is produced in waste amounts from breweries and is the main source for NADH production. The NAD extracted from yeast is reduced to NADH in a natural way by an enzyme isolated also isolated from yeast.

DIETARY SOURCES OF NADH

NADH is present in every living cell of animals and plants, so it readily occurs in the foods we eat on a daily basis. Meat and fish contain the highest amounts of NADH. Meat is nothing but muscle tissue, which is used for movement, force, and power. Muscles need energy for these actions and they get it from NADH. Meat contains about 50 milligrams (mg) of NADH per kilogram. In liver tissue, you will find about 11 mg of NADH per kilogram. NADH also occurs in fruits and vegetables, but the content is far lower than in animal tissue, because plants need much less energy than animals.

Though NADH is present in our foods, we take up only marginal amounts of it from our daily diet. Most of the NADH is destroyed during the cooking process. The situation would not be much improved even if our diet consisted mostly of raw meat and fish as the NADH present in these foods is degraded within seconds by the acid environment produced by our gastric juices in the stomach. However, NADH is synthesized in the cells from simple molecules such as glucose (sugar) and amino acids.

NADH CONTENT IN FOOD	
FOOD	**AMOUNT OF NADH (IN MG/KG)**
Meat	50
Fish	35
Liver	11
Corn	1.8
Carrots	0.46
Potatoes	0.2
Onions	0.41
Blood (human)	7.5

NADH IS PRODUCED IN THE BODY

Our daily food consists of carbohydrates, proteins, and fat. These large molecules are degraded by enzymes into smaller entities such as sugar, amino acids, and fatty acids. These compounds are then transported from the blood circulation into the organs, where they are taken up by the cells. There they are split further and inserted in the citric acid cycle, also called the Krebs cycle (named after the German biochemist and Nobel laureate Sir Hans Krebs). In this metabolic roundabout, the hydrogen is taken from the glucose and transferred to NAD. By this mechanism, NADH is formed. It then reacts with oxygen to produce ATP and water.[2]

ATP, the abbreviation of adenosine triphosphate, is a special molecule that has energy stored in its chemical structure. When ATP reacts, this energy is released and used for production processes in the cells of the body.

NADH occurs in relatively high amounts in the human body. The highest content of NADH is found in the heart as it needs the most energy;[3] it beats 86,000 times per day. Here are NADH concentrations in various human organs and tissues:

- Heart, 90 mg/kg tissue
- Liver, 11 mg/kg tissue
- Muscles, 50 mg/kg tissue
- Erythrocytes (red blood cells),
- Brain, 40 mg/kg tissue 8 mg/kg tissue

The brain consumes one-third of all the energy produced by our body. Therefore, an energy deficiency is first detected in the brain. Attention deficit, weaknesses in focusing, and prolonged reaction times are all caused by too little ATP in the brain. A long-term energy deficiency in the brain leads to a shortage of the neurotransmitters, noradrenaline, dopamine, and serotonin.[4] If this condition persists for a long period of time, symptoms of depression such as loss of drive, sleep disturbances, hypochondria, and anxiety will develop.

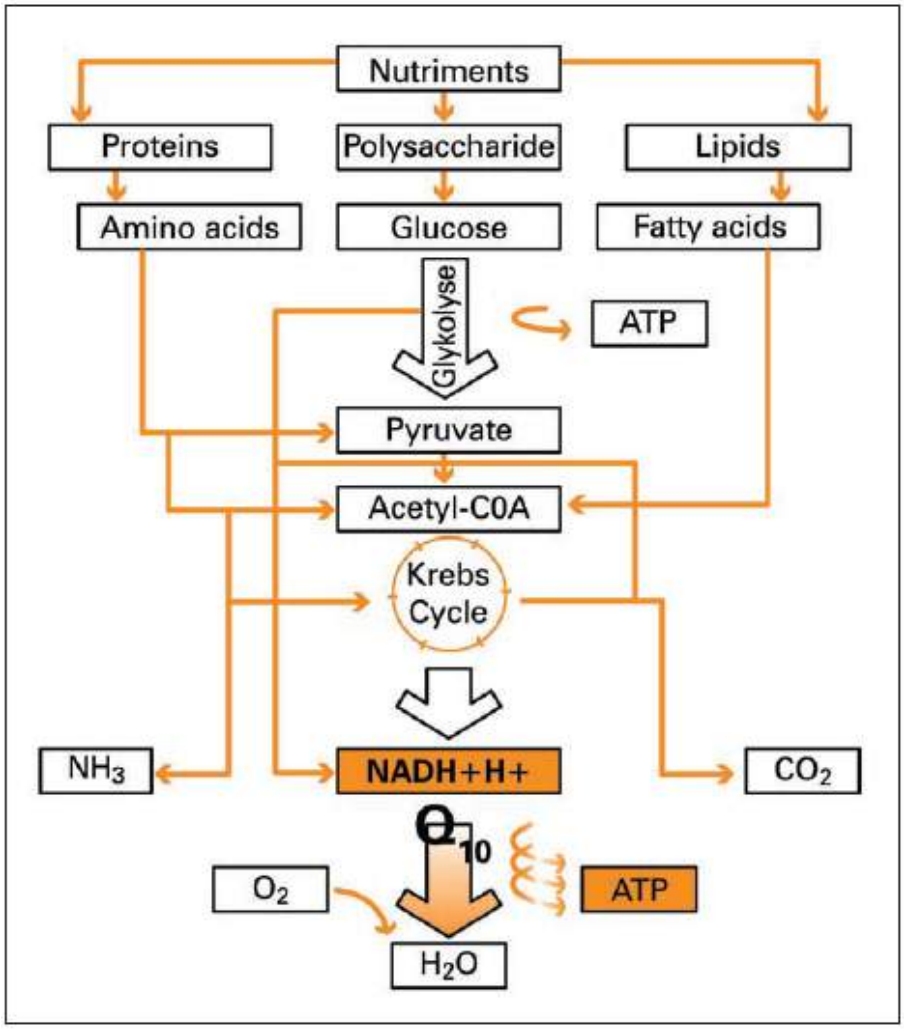

Figure 1.1. NADH production in the cell.

NADH has numerous biological functions in the human body. It catalyzes more than a thousand metabolic reactions in the various tissues and organs, the most important of which are explained in the next chapter.

CHAPTER 2

Functions of NADH in the Body

THE CELLULAR FUEL

The billions of cells that the human body is composed of absolutely need one thing—energy. Without energy, a cell cannot survive. Each cell must produce the fuel on its own. What is this fuel? It is hydrogen that reacts with oxygen in the cell to produce water and energy.

As you may know, liquid hydrogen and liquid oxygen are used as rocket fuel. When they are blended together, an explosion is triggered that boosts the rocket into the sky. How does the cell tame this highly reactive hydrogen? The cell is very sophisticated in doing this. The hydrogen is coupled to a larger molecule, namely NAD. In this biological form, the amount of hydrogen is less but it is sufficiently reactive to combine with oxygen to form water and energy.

The still high reactivity of the biological hydrogen in NADH is one of the reasons why it has never been considered for therapeutic application. As I will explain later, I succeeded in taming this biological rocket fuel and transposing it into a compound usable for therapeutic applications. This biological form of hydrogen reacts with oxygen not in an explosive manner but in a cascade of controlled biochemical reactions. Water and energy are formed and this energy is stored as adenosine triphosphate (ATP). Biochemists call this process “oxidative phosphorylation” because the cell needs oxygen for this reaction.

ATP is the life energy for every cell. The more a cell has available, the better it functions and the longer it lives. If cells of a tissue or organ stay vital longer, the organ and the entire individual survives longer.

How can an ATP deficiency develop? It is comparable to a state budget. Either its income is too low or expenses are too high. In most states, both reasons are the cause of the deficit. So it is in the cell—both possibilities may be the cause. NADH is produced by the cell from glucose, amino acids, and fatty

acids. If the production chain for these building blocks is disturbed, less NADH is formed. If less NADH is present in the cell, less ATP is synthesized. If the ATP content of a cell falls below a critical value essential for life, the cell dies.

So, each cell needs adequate amounts of NADH and oxygen to be able to produce sufficient amounts of ATP. If the enzymes catalyzing the transformation of NADH and oxygen to ATP are inhibited or destroyed by chemical or physical agents, less or no ATP is produced. As a consequence, cells and tissues will die.[1]

Special and ubiquitous inhibitors of these enzymes are free radicals, which are reactive molecules that are detrimental for cellular energy production. We are constantly exposed to rather high amounts of free radicals in form of sunlight (UV radiation), radio waves, ozone, cigarette smoke, drugs, and other chemicals we are using on a daily basis. Today, it is generally accepted by the scientific community that certain diseases—particularly neurodegenerative conditions such as Alzheimer‘s dementia, Parkinson’s disease, and muscular dystrophy—are caused by an impairment of the ATP-producing enzymes.[2]

To protect ourselves from the many toxins we are exposed to we need to increase the ATP production in our cells. With more ATP, the cell will function better and survive longer. We can increase the ATP content in a cell by supplementing with NADH.

NADH INCREASES ATP IN HEART CELLS

That NADH can increase ATP levels in heart cells was demonstrated by studies at the University of Graz in Austria. Scientists from the departments of medical chemistry and physiology isolated heart cells and exposed them to NADH. That is, the NADH was added from outside these cells. After an incubation time of 4 hours, an increase of NADH and ATP inside the cells could be detected.[3]

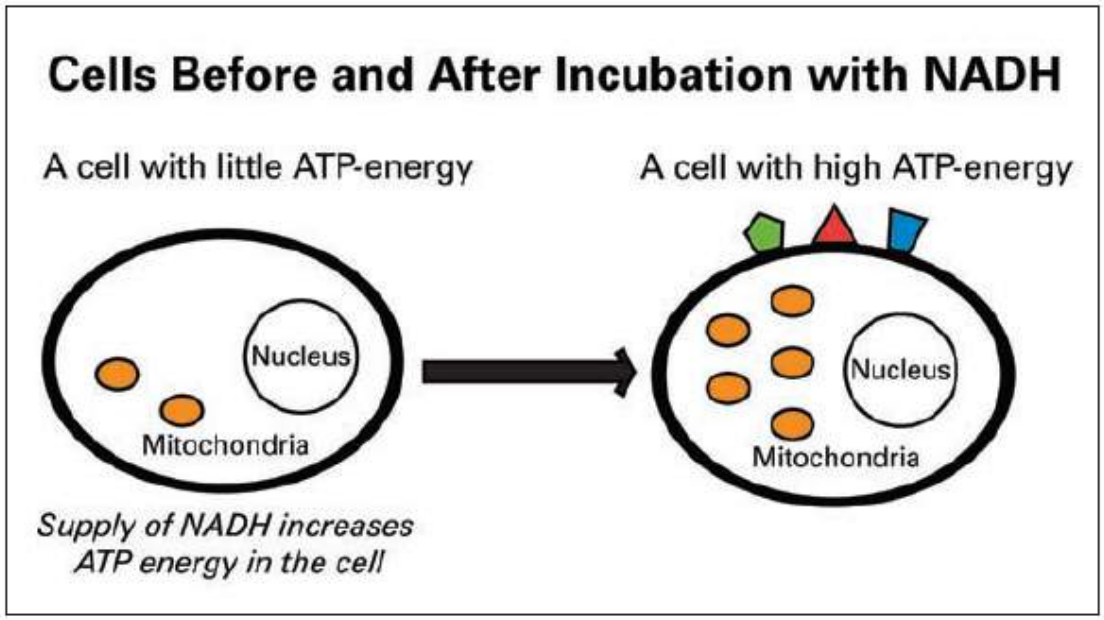

Figure 2.1. ATP level in heart cells before and after incubation with NADH.

These experiments proved that NADH is able to get into the cell by passing through the cell membrane. Before this conclusive experiment was performed, all biochemistry textbooks stated that NADH cannot diffuse through the cell membrane and that all the NADH needed by the cell must be produced exclusively inside the cell. NADH is taken up by the mitochondria, the power plants of the cells, and there the reaction between NADH and oxygen occurs, which leads to the production of ATP. These heart cell experiments revealed not only an increase of NADH in the cells but also an increase of ATP when the cells are exposed to NADH. More NADH in the cell leads to more ATP. By this process, the cell gains more energy and functions better. This sensational discovery has enormous implications for all organs, in particular for the heart and the brain.

NADH PROTECTS AND REPAIRS DNA

The information center of every cell resides in the DNA (deoxyribonucleic acid), the genetic blueprint located in the nucleus. As these components are of utmost importance for the cell, they are protected by "body guards"—big protein molecules called his-tones, which bind to the DNA forming a kind of coat. Only during cell division is this coat displaced in order for the DNA to be able to replicate.

During cell division or when the protective coat is damaged, the DNA can be altered by influences outside the cell, such as radiation, ozone, and chemical toxins. The human body is constantly exposed to all of these. It is important to note that the chemical industry produces more than 20,000 new chemicals every year, often without knowing how potentially toxic they are. Most of them go into use without being tested for their toxicity.[4] Herbicides, insecticides, cleaning products, and lacquers are just a few of these products. People are exposed more than ever before to new potentially toxic substances and their damaging effects on the organism are barely known. These toxins are taken up by the body and react with the chromosomes in the nucleus of the cell leading to altered DNA. The greater the damage in the DNA, the more extensive are the alterations in the cells and in the tissues.

These DNA mutations are the biochemical cause for numerous diseases, such as cancer, arteriosclerosis, immunodeficiencies, rheumatoid arthritis, and diabetes.[5] So, it is imperative to protect the DNA and prevent replication of altered and damaged DNA. For example, if this occurs with heart cells, which contract spontaneously every second, they lose their ability to do so. The consequence is an insufficiency in the heart at the cellular level. Fortunately, this is rarely the case—only if the heart is intoxicated by drugs such as doxorubicin. The cells from the intestinal mucosa are renewed every 3–4 days; this frequent rate of cell division represents a much higher risk for a DNA alteration and also a greater hazard for the development of cancer.

As damage to the DNA could lead to fatal consequences, both mammalian and human cells have developed a system to repair alterations to their genetic material. This so-called DNA

repair system is based on enzymes that are able to correct the changes or errors in the DNA.[6] Damaged DNA is comparable to a zipper in which a couple of teeth are missing and therefore does not work. The repair enzymes integrate the components absent in the altered DNA. As an essential cofactor, these repair enzymes need NADH.[7]

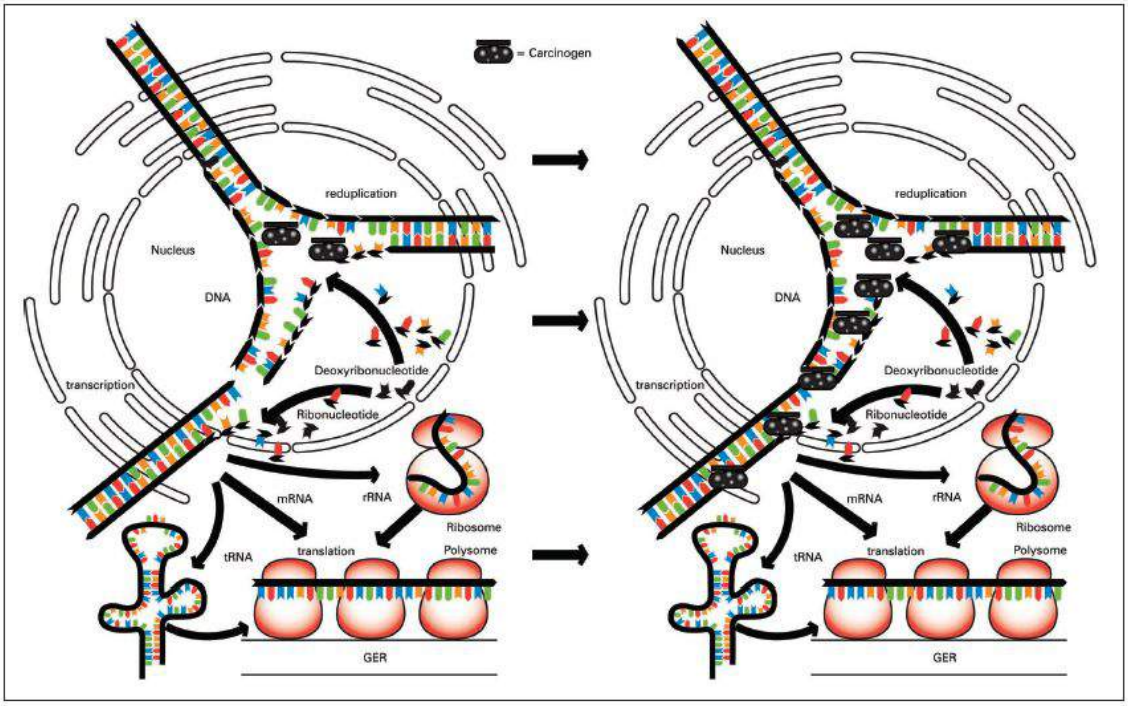

Figure 2.2. Carcinogen damage.

Scientists at the University of Guangzhou in China documented that damaged DNA can be repaired by NADH. In one experiment, they used doxorubicin, a toxic cytostatic drug frequently used for cancer therapy. Doxorubicin damages DNA but this is actually the therapeutic concept of cytostatic drugs —to damage the DNA of cancer cells so that they die off. However, they do not act selectively on cancer cells but also damage normal cells. Therefore, chemotherapy causes side effects and adverse reactions unless normal cells can be protected.

This appears to be possible. Cells were incubated with doxorubicin, which damaged the DNA. Then the cells were treated with NADH and the DNA damage was repaired. The mechanism of repair appeared to be based on the action of certain proteins, such as cyclin A, cyclin B1, p53, and Bcl-2, which all play a central role in the regulation of cell division.[8] NADH is now being used as an adjunct therapy with cancer patients to

protect the normal non-cancerous cells from the damaging action of chemotherapy. NADH is also capable of protecting cells from apoptosis, also known as programmed cell death.[9]

NADH REVITALIZES DAMAGED CELLS

NADH can revitalize cells that have been damaged by exposure to radiation. In one experiment, liver cells were exposed to extreme high-voltage x-rays, leading to such enormous damage that these cells should not survive and would die soon. When these severely damaged cells were incubated with NADH, 70 percent of the cells could be repaired and rendered fully functional again. If the cells are exposed to NADH before they are exposed to x-rays, NADH protects them against the damaging effect of the radiation.[10]

The illustration below shows electron microscopic pictures of liver cells after exposure to radiation, both before and after treatment with NADH. The upper left photo (A) shows normal liver cells before radiation. All the cell structures, such as the nucleus and particularly the cell membrane, appear intact. After radiation with x-rays, the cells look severely damaged (B and C): the nucleus appears altered and the cell membrane is leaky and partially destroyed. After incubation of the damaged cell with NADH, the cells appear normal (D), comparable to picture A: the nucleus and the cell membrane seem to be intact as before the radiation.

NADH has a scientifically proven, strong, and very specific protective effect. It defends the cells against the destructive influence of any kind of agent, such as radiation, environmental pollutants, drugs, and chemicals.[11]

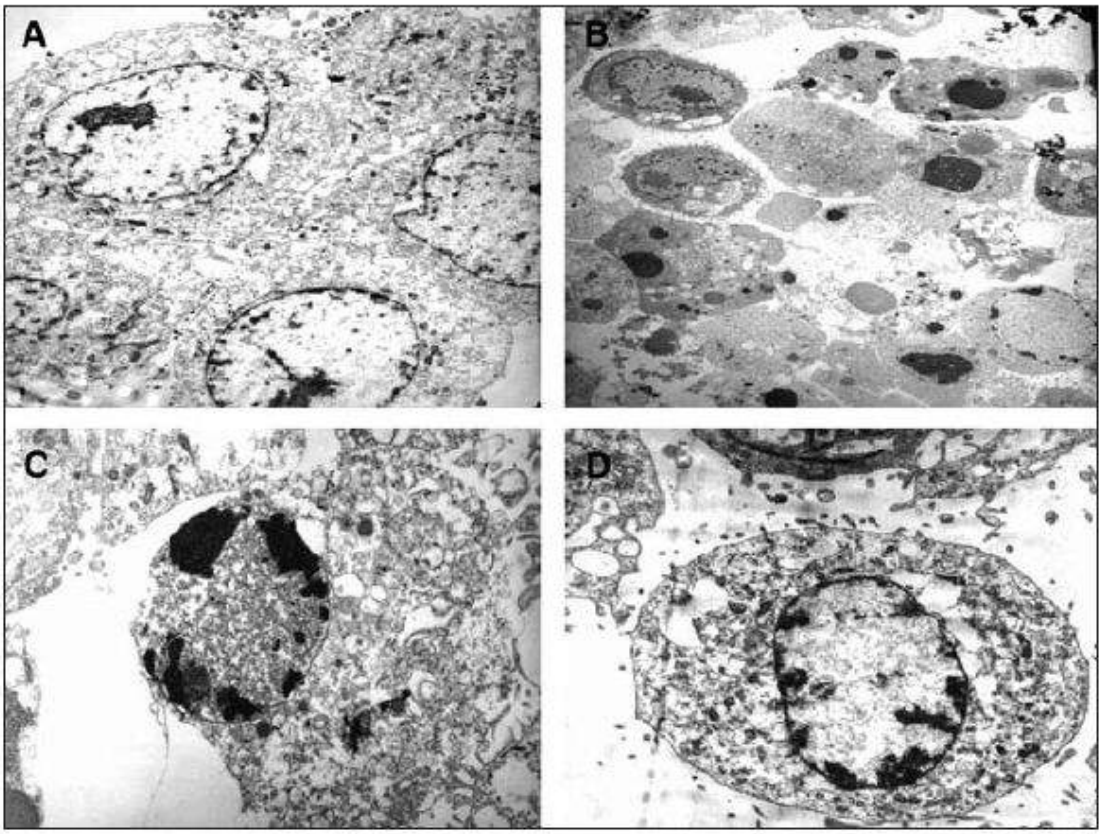

Figure 2.3. Electron microscopic pictures of liver cells after exposure to radiation, before and after treatment with NADH.

NADH IS A POTENT ANTIOXIDANT

An antioxidant is a compound that acts against oxidation. If iron gets oxidized, iron oxide is formed, which most people know as rust. Oxidation is a phenomenon we see in many areas of our life. Fats such as butter get rancid and so do foods. It is nothing but oxidation. This same process happens to tissues in the body. While we need the oxygen from the air to survive, this oxygen makes stuff rusty or rancid. The opposite of oxidation is reduction—a chemical compound having a strong reducing power acts as a potent antioxidant.

NADH has the highest reduction potential of all biological molecules of a cell.[12] Therefore, it is one of the most potent biological antioxidants. Other well-known antioxidants are vitamins A, C, and E, as well as selenium and glutathione. Also, the enzymes glutathione peroxidase and superoxide dismutase exhibit antioxidative properties in every living cell.[13]

The strongest enemy of antioxidants are free radicals. These are extremely reactive molecules that attack almost all components of the cells in our body. They alter the lipid structure of the cell membrane, making it leaky;[14] as a consequence, the cell dies. Free radicals also attack the DNA and proteins, damaging enzymes involved in metabolic reactions. Important cellular functions become impaired as a consequence. Free radicals are regarded as one of the causes of coronary heart disease, cancer, arteriosclerosis, diabetes, and neurodegenerative diseases (Parkinson's and Alzheimer's disease).[15] Free radicals can arise from x-rays, UV light, ozone, pollution, toxic metals, alcohol, and cytostatic or antibiotic drugs.

The human body has developed a defense system capable of destroying these aggressive "cell destructors." This antioxidative defense shield is able to neutralize a certain amount of free radicals. If our body is exposed to too high amounts of free radicals, this protective barrier is overstrained resulting in damage to tissues and organs. Therefore, it is necessary to supply the body with sufficient amounts of antioxidants to strengthen the defense shield against free radicals.

NADH regenerates the antioxidative capacity of other components in the cell. This function is particularly important for coenzyme Q_{10} (CoQ_{10}). This coenzyme plays an important role

for the energy production in the cell. However, CoQ_{10} needs NADH to be transformed into its active, reduced form. If coenzyme Q_{10} is not present in its reduced form, it does not act either in energy production or as an antioxidant. CoQ_{10} is converted to its active, reduced, form only inside the cell by NADH. Without NADH, CoQ_{10} cannot work, whereas NADH does produce energy in the cells even without CoQ_{10}. People taking cholesterol-lowering medications should be aware that these drugs not only suppress the production of cholesterol but also of CoQ_{10}. A deficit of CoQ_{10} can cause cell death and destruction of tissue. If a physician recommends that you take cholesterol-lowering drugs, you should always take CoQ_{10} as an additional supplement and also NADH to activate the CoQ_{10}.

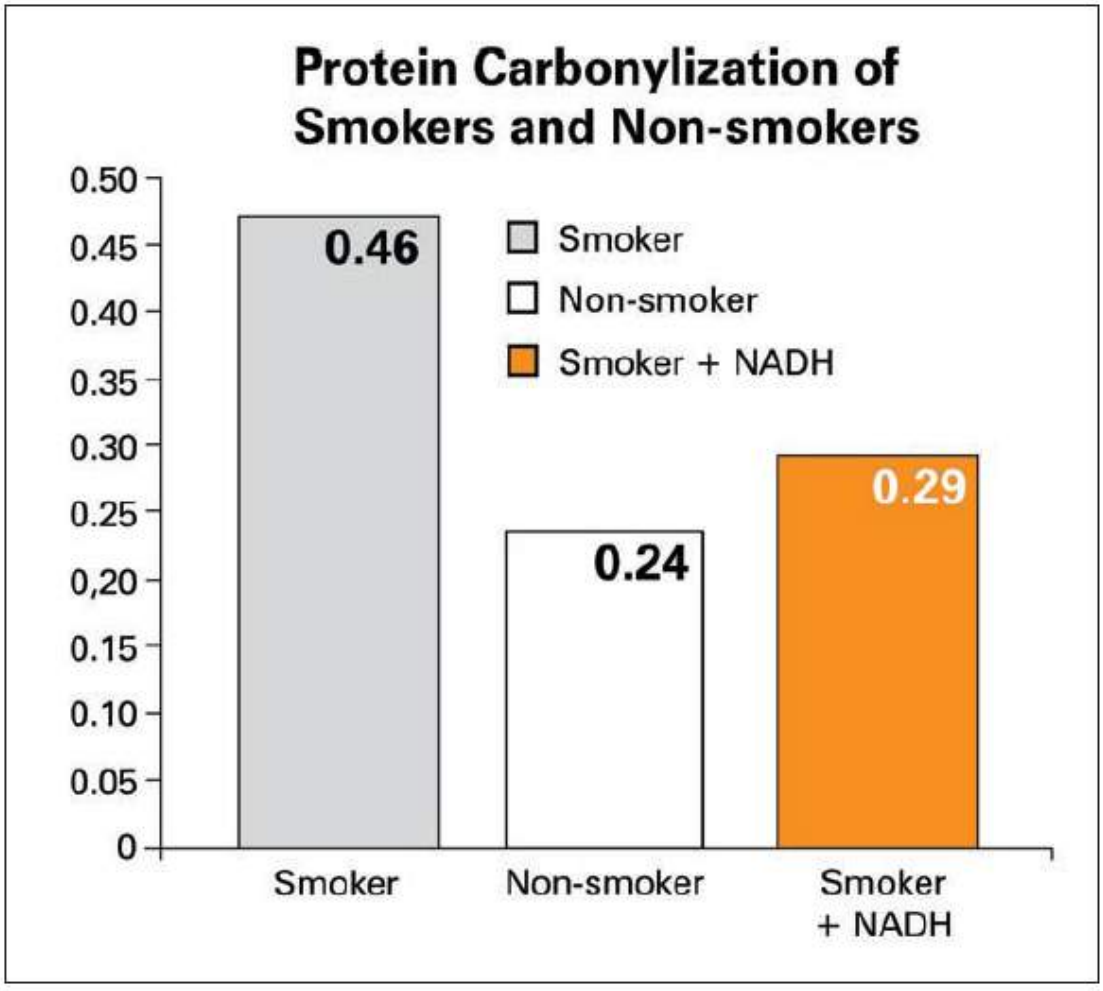

Figure 2.4. Protein carbonylization.

The antioxidative capacity of NADH was investigated at the University of Graz, in Austria. This was not done experimentally in the test tube but with actual students. In a double-blind, placebo-controlled study with thirty-seven healthy students at the medical school, parameters indicative for damaging oxidative reactions (such as malondialdehyde) were measured in the blood of the subjects before and after intake of NADH. The more malondialdehyde found in the blood, the more severe is the oxidation of the lipids in the tissue. After intake of NADH, malondialdehyde levels in the blood declined.[16] The oxidation of LDL (so-called bad) cholesterol is regarded as a trigger for arteriosclerosis. Oxidized LDL cholesterol was also significantly reduced after intake of NADH.

Proteins modified by oxidative stress can be also used as an indicator for the effects of free radicals on our body. Preliminary studies indicate that the modification ("carbonylization") of these proteins is highly elevated after smoking. Smokers taking NADH before each cigarette have elevated levels of modified proteins, but only about 25 percent higher than that of nonsmokers. Compared to smokers who didn't take NADH, the damage of smoking can be reduced by 75 percent by taking NADH orally.[17] Based on this observation, smokers can protect their body, particularly their lungs, from much of the harmful action of cigarettes by taking NADH.

NADH LOWERS CHOLESTEROL

In a double-blind study, scientists at Georgetown University, in Washington, D.C., found that NADH lowers cholesterol.[18] One group of rats was given a daily dose of NADH (5 mg) for eight weeks, while another group of rats received a placebo. Two months later, the level of total cholesterol decreased by about 30 percent and so did the concentration of LDL cholesterol.

These findings were confirmed in another study by researchers at NUMICO, in the Netherlands. NUMICO is the producer of the baby food Milupa. In the study, rats were given one tablet (5 mg) of NADH for eight weeks. The total cholesterol decreased by an average of 10 percent. The scientists also found that the contraction force of the aortic ring near the heart increased after the NADH treatment. This observation indicates that NADH can strengthen the power of the heart muscle as well as that of the aorta.

At this time, we have no insight into the mechanism by which NADH lowers cholesterol. However, this coenzyme could certainly be one of the best and safest cholesterol-lowering compounds and, as a biological substance, free of side effects.

NADH LOWERS HIGH BLOOD PRESSURE

Many of my patients taking NADH on a regular basis have reported that their blood pressure was lower than before taking this coenzyme. These hints spurred us to look further into this blood pressure-lowering effect of NADH. A study was organized at Georgetown University with spontaneous hypertensive rats. These animals develop high blood pressure very early in life and are used regularly for testing antihypertensive drugs. The researcher at Georgetown measured the blood pressure of the rats before and eleven weeks after giving the rats NADH (5 mg per day). Blood pressure decreased by 10 percent after the NADH treatment, whereas the animals receiving the placebo did not show a decline.[19]

NADH BOOSTS THE IMMUNE SYSTEM

The immune system is composed of the cellular and the humoral system. The first is based on the activity of specific white blood cells: T-lymphocytes, B-lymphocytes, and macrophages. Macrophages are responsible for the direct elimination of bacteria, viruses, and other foreign bodies. They take them up and degrade them, a process comparable to eating and digestion, which is why they are called phagocytes.

The first step in the elimination of bacteria is the perturbation of the plasma membrane of the phagocyte cells. As a consequence, the metabolic activity is markedly increased, including the oxygen consumption within the cells. Most of the oxygen is converted to superoxide and hydrogen peroxide.[20] This phenomenon, known as the metabolic burst, appears to be the first and most critical step leading to the destruction of the invader. During this metabolic burst and in the cytotoxic (cell killing) activity of the macrophages, high amounts of NADH are used. The logical conclusion is that the more NADH the body has available, the better the cellular immune system works. The stimulatory effect of NADH on the immune system has been demonstrated with human white blood cells—that is, their function can be optimized by NADH.

Lymphocytes and macrophages send out signals to each other, communicating how and where they should become active. The signals are based on the action of proteins called cytokines, which transmit the information from one cell type to the other (for example, from T-lymphocytes to B-lymphocytes). These messenger substances include various interleukins and interferons to establish the communication between the white blood cells.

In collaboration with a research group at the University in Berlin, we found NADH to stimulate the biosynthesis of interleukin-6 above the normal concentration in a dose-dependent manner.[21] A number of scientific publications indicate a protective effect of interleukin-6 on nerve cells damaged in various ways. In certain neurodegenerative diseases, such as Alzheimer's disease, Parkinson's, and multiple sclerosis, the concentration of interleukin-6 is considerably reduced. So,

NADH may be a useful tool to overcome this shortage of interleukin-6.

NADH STIMULATES ADRENALINE AND DOPAMINE

The first indications that NADH had a stimulatory effect on adrenaline and dopamine biosynthesis were derived from studies involving patients with Parkinson's disease in the late 1980s. Parkinson's disease is characterized by three major symptoms: tremor, rigidity, and akinesia (immobility). The biochemical cause of this disease is a lack of dopamine production in a specific area of the brain. Dopamine is a neurotransmitter essential for the coordination of mobility and movement. Neurotransmitters are signal molecules that trigger certain reactions in nerve cells.

Mobility improved considerably in the first application of NADH in a Parkinsonian patient. Before the NADH infusion, the patient had difficulties in getting up from his chair and could only walk in small, tripping steps. One hour after NADH infusion (20 mg), the patient could get up from his chair without any problems, could walk normally, and could even jump. This was the very first hint that NADH stimulates dopamine biosynthesis in the brain. A couple of years later, this NADH effect was proven on isolated nerve cells.[22] In these experiments, NADH was added to the liquid solution in which the nerve cells had been grown. The result was a dose-dependent increase in dopamine production (up to a sixfold increase). In addition, an elevation in the activity of tyrosine hydroxylase—the enzyme responsible for dopamine biosynthesis—was also observed.

These findings were confirmed by studies at the University in Paris. French scientists injected NADH daily into rats. Then, they determined the concentration of dopamine and noradrenaline in specific areas of the brain, both before administration of NADH and four weeks after the daily injections began. After four weeks, they found a 40 percent increase of dopamine and noradrenaline levels in specific brain areas.[23]

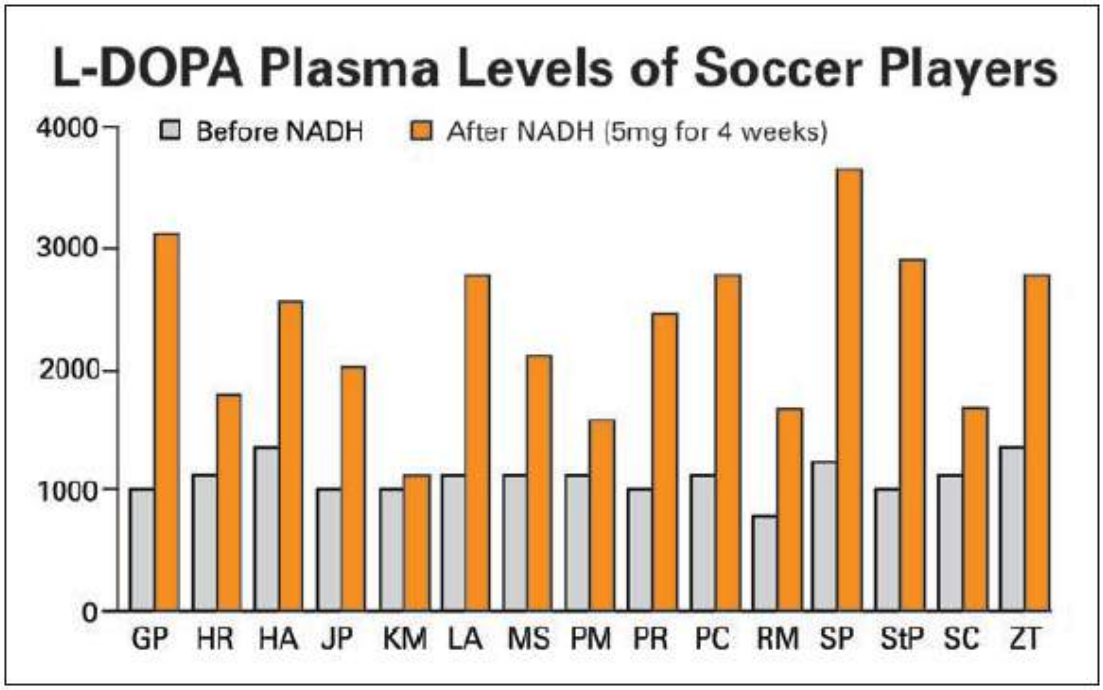

Figure 2.5. Dopamine levels before and four weeks after NADH.

NADH leads also to an increase in blood dopamine levels in healthy individuals. This was shown with professional athletes who took NADH (5 mg per day) for four weeks. The dopamine level increased by an average of 50 percent in all athletes, and noradrenaline levels also increased in all but two of the athletes. Based on these findings, NADH can have a positive effect on all physiological functions triggered by dopamine and adrenaline. These include mobility, coordination, power, alertness, and cognitive processes, as well as mood and sense of well-being.

Dopamine also has a substantial influence on sexual behavior, particularly on libido. Because Parkinsonian patients suffer from a lack of dopamine, many patients complain about disturbance in their sex drive, such as lack of orgasm and ejaculation problems.[24] NADH may be useful in helping patients overcome these difficulties. The stimulatory effect of NADH on libido has been confirmed by many Parkinson's patients who have taken NADH regularly for a long period of time.

Furthermore, dopamine lowers the secretion of prolactin and reduces appetite. The higher the dopamine level, the lower the appetite. This effect may have some importance for overweight people, as NADH can be taken as a dietary supplement. The positive influence of dopamine on the secretion of human

growth hormone should also be mentioned. This hormone plays a key role in the regeneration of cells and tissues.[25]

NADH AND NITRIC OXIDE (NO)

Nitric oxide (NO) was detected in the human body only a few years ago. NO has a number of functions in the body. It transmits information from one nerve cell to another, thus acting as a neuro-transmitter.[26] NO also influences the immune system and inhibits the aggregation of the blood platelets, which seal damaged blood vessels and stop bleeding. Aggregation of blood platelets in a vessel can lead to circulation blockage; if this happens in the brain, a stroke is the consequence. Substances such as nitric oxide, which inhibit aggregation, may be a useful tool for the prevention of stroke or heart attack. One of the other important physiological effects of NO is the relaxation and dilatation of blood vessels.[27] Due to this phenomenon, all organs get more blood—more blood means more oxygen, more nutrients, and a better functioning of the cells.

Nitric oxide is formed in the cells from the amino acid arginine by the enzyme nitric oxide synthase.[28] The coenzyme of the nitric oxide synthase is NADH, so the more NADH the body has available, the more NO can be formed. Needless to say, a sufficient amount of arginine must be present as well. (An arginine deficiency in the body can be overcome by taking this amino acid in pure form as a dietary supplement.) Researchers from the University of Ohio found that NADH can stimulate the formation of NO in the cells in a dose-dependent manner. They found that NADH promotes NO production more than any other substance.

In addition to its effects on nitric oxide, NADH functions as sensor of blood flow in the brain, muscles, and other tissues, particularly when the organs are active and need more oxygen. The mechanism of this action is regulated by oxygen and nitric oxide.[29] The blood vessel–relaxing effects of NO induced by NADH has medical relevance for angina, asthma, and migraines. Also, the reproductive organs of men and women benefit from the greater blood supply triggered by NADH.[30]

CHAPTER 3

Supplementing with NADH

Based on the various physiological effects of NADH, described in the last chapter, men and women are better protected against health problems the more NADH they have available in their bodies. Can we increase the NADH content in the body? Yes, we can as safe and effective NADH supplements are now available.

DEVELOPMENT OF AN NADH SUPPLEMENT

After many years of extensive research, I succeeded in developing a formulation in which NADH is stabilized and absorbable by the intestinal tract. NADH as the biological form of hydrogen is very reactive—it is oxidized to NAD rapidly by air and oxygen. This was one of the reasons why NADH had never previously been considered for therapeutic application.

In 1987, my late father, Professor Walther Birkmayer, infused NADH into a patient with Parkinson's disease. The therapeutic effect was instantaneous and impressive: the patient, who had problems even getting up from his chair and walking, could do so only an hour after receiving NADH. This was the very first injection of NADH and revealed that it could be used therapeutically.

Based on this observation, a couple of hundred Parkinsonian patients were treated by NADH infusions. However, this treatment was possible only in our clinic, the Birkmayer Institute for Parkinson Therapy, in Vienna. The many patients coming from abroad had no access to NADH infusions when they went back home. So, many of these patients expressed the desire to have NADH available as a tablet. This started me on the path to develop an oral form of NADH.

The development of oral NADH tablets turned out to be much more difficult than I had originally thought. It took almost five years until I found a formulation in which NADH is stable. The reason for these difficulties was the hydrogen in NADH, which renders it unstable. It appeared almost impossible to make a tablet in which NADH is stable for more than two years, the prerequisite period for approval of a substance as a drug.

In the first experiments, I blended NADH with lactose, the most commonly used filler for tablet compression. The powder was then compressed into tablets. Four weeks later, we analyzed the NADH content and found no NADH in the NADH-lactose tablets! Obviously, the NADH had re-

acted with the lactose (even in the dry powder form of the tablet). After months of searching for another filler material, we found one that worked—mannitol. Mannitol is a natural, nontoxic sugar alcohol that is used as sweetener in a number of food products, such a chewing gum or lozenges. NADH did not react with mannitol and the stability of NADH could be extended considerably, but not long enough to fulfill the minimum two-year requirement. After a series of time-consuming experiments, I found an additional stabilizer for NADH: sodium bicarbonate (baking soda), at a distinct concentration, renders NADH stable for more than two years.

For this special formulation of NADH with mannitol and baking soda, I obtained a number of international patents.[1] In order to receive patents for the stabilization of NADH in tablet form, we had to document the proof for it to the patent office. The NADH content in the tablets was analyzed and results confirmed the NADH content remained unchanged after two years.[2]

BIOAVAILABILITY OF NADH

A number of critical biochemists raised doubts about whether NADH can be absorbed at all by the intestinal tract. They argued that NADH is oxidized and degraded before being absorbed. In a doctoral thesis for the Free University, in Berlin, scientific evidence was obtained that NADH taken orally penetrates the intestinal mucosa undegraded and reaches the blood circulation.[3] Pharmacokinetic investigations recently performed on NADH have confirmed the previous study showing that NADH is absorbed in the gut.[4]

NADH is also absorbed by the oral mucosa if the tablet is dissolved under the tongue. The bioavailability of NADH after sublingual application was proven using laser-induced fluorescence. When a rat receives an NADH tablet under the tongue, a significant increase of the NADH fluorescence in the brain cortex of the animal can be measured 15 minutes after application.[5]

These results also show that NADH can pass the blood-brain barrier. More NADH in the brain means more ATP energy and better cognitive performance. The increase in ATP production in the brain, and the metabolic processes triggered by it, represent the basis for the therapeutic effect with neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, and multiple sclerosis.

NADH DOSAGE

The maximum tolerable dose (MTD) is the amount of substance that can be tolerated by a receiver without symptoms of intoxication or persisting damage to health. For determining the maximum tolerable dose, NADH was given intravenously in increasing doses to rats. The MTD of NADH was found to be 500 mg per kilogram of body weight. If this value is adjusted for a person weighing 70 kilograms (154 pounds), the amount is 35,000 mg (35 grams). This corresponds to a volume of 5 tablespoons of NADH (or 3,500 tablets containing 10 mg of NADH) that could be taken without complaints or harmful effects.[6]

Tests for subacute toxicity levels of NADH, performed in beagle dogs, found that after fourteen days of daily oral doses of 150 mg/kg of NADH, no changes in the organs and tissues of the dogs were detected. That means a 10-kg (22 pound) dog can tolerate 150 tablets per day of 10-mg NADH. Health authorities also request data on long-term (over a period of six months) observations for potential side effects (chronic toxicity studies). In these studies, rats given one tablet (5 mg) per day of NADH for six months showed no changes, either macroscopically nor microscopically, compared to animals receiving a placebo.[7]

Calculating the equivalent daily dose for a human (70 kg body weight), an amount of 1050 mg is obtained. Divided by the NADH content of one tablet (10 mg), the number of tablets that a person could take on a daily basis for twenty-six weeks (half a year) without any harm is 105 per day. Based on this scientifically proven, enormously high tolerance, NADH is certainly one of the safest dietary supplements, much safer than many multivitamins, minerals, or trace elements.

A healthy person should take 2 tablets per day as an energizing potion and as prevention for ailments. The tablets should be taken on an empty stomach with a glass of water about 20 minutes before a meal or 2 hours after a meal. According to our experience, elderly people prefer to take

the NADH tablets first thing in the morning, while younger folks take it in the early afternoon to keep the energy boost going longer in the day. There is no harm when the tablets are taken with meals. However, the NADH may react with the food and may reduce the efficacy of it to a certain extent. People with fatigue or recovering from an ailment should take at least 4 NADH tablets per day, two in the morning and two in the early afternoon.

SIDE EFFECTS WITH NADH

The patented NADH formulation that I developed has been marketed as a dietary supplement in the United States for almost ten years and many Americans have taken this product regularly during that time. Up to now, the companies selling our NADH product in the U.S. have not received any report about a side effect.

Potential side effects must be documented in all clinical trials. Studies with NADH have been performed at a number of research institutions, including Georgetown University, Washington, D.C.; Cornell University, New York; Institute for Sports Medicine, University of Freiburg, Germany; Birkmayer Institute for Parkinson Therapy, Vienna, Austria; First Military University, Guangzhou Hospital, China; and Institute for Medical Chemistry, University of Graz, Austria. No side effects have been observed during all of these studies. For example, in the study performed at the University of Freiburg, highly conditioned athletes were taking 30 mg of NADH per day for one month. Even at this dose, which is four times the recommended daily dose of 7.5 mg of NADH, no side effects were observed.

During the clinical study performed at Georgetown University, which involved patients suffering from chronic fatigue syndrome, they continued with their other daily medications. Many of those patients were taking blood pressure medication, anti-allergy medicine, antidepressants, blood thinners, or cholesterol-lowering drugs. The physicians examining the CFS patients did not receive reports that NADH had interacted with, or altered the effect of, the drugs they were taking. Furthermore, the more than 10,000 consumers of NADH, who were regularly taking medications prescribed by their physicians, have not reported any influence of NADH on the effect of their medication.

CHAPTER 4

NADH and Disease Treatment

NADH has proven useful in treating a number of conditions, including Parkinson's disease, depression, chronic fatigue syndrome, Alzheimer's dementia, cancer, strokes, and diabetes.

PARKINSON'S DISEASE

The story of NADH as a new therapeutic approach is intricately linked to my late father, Professor Walther Birkmayer. In 1987, he used NADH for the first time as an intravenous infusion in a patient with Parkinson's disease. His medical career began at the end of World War Two. In Vienna, he became chief physician at the Hospital for the Brain Injured (*Wiener Hirnverletzten-Lazarett*), where he saw over 3,000 brain-injured patients. He concluded that brain damage leads to a disproportion of certain neurotransmitters. These substances transmit information from one nerve cell to another and can trigger symptoms and alterations in behavior.

Analogous changes in the balance of the neurotransmitters adrenaline, dopamine, and serotonin were found in the brains of Parkinsonian patients. In 1957, Professor Arvid Carlsson discovered that mobility and physical power in animals was related to the neurotransmitter dopamine: the higher the concentration of dopamine in the body, the greater the vigor and muscle tone. Dr. Carlsson demonstrated this phenomenon with a simple experiment. He withdrew dopamine from rabbits by injecting them reserpine, a medication used at that time for reducing blood pressure. The lack of dopamine changed the behavior of these animals—they hung their ears and were slack and weak. Then, he injected them with dopamine and in seconds the rabbits stretched their ears and were back on track, full of vigor and tension.[1] Based on his observations, Dr. Carlsson postulated that dopamine played a role in Parkinson's disease. For his research in the field of neurotransmitters, Dr. Carlsson was awarded the Nobel Prize for Medicine and Physiology in 2000.

From Dr. Carlsson's research, my father deduced that Parkinsonian patients had a dopamine deficiency in the brain, and he was convinced that this deficit caused the symptoms of the disease. If true, Parkinson's symptoms, such as rigidity and impaired mobility, should improve by injecting dopamine. Dopamine is a neurotransmitter responsible for muscle tone, tension, and physical strength, as well as for emotions including sex drive (libido).

The control center for movement, coordination, and power of the body is located in the black substance (substantia nigra), a pea-sized tissue in the basal part of the brain. The characteristic symptoms of Parkinson's disease are rigidity, tremors, and immobility. These symptoms become obvious only after half of the black substance in the brain is already destroyed and the production of dopamine has declined by at least 50 percent. Trembling is the first hint with many Parkinsonian patients.

Research Breakthroughs in the Treatment of Parkinson's

In 1961, my father injected L-DOPA (L-dihydroxyphenylalanine) for the first time in a Parkinsonian patient who was bedridden and unable to get up. A few minutes after the infusion, the patient could get up from bed and walk. L-DOPA was injected rather than the missing dopamine because dopamine cannot pass the blood brain-barrier. L-DOPA, on the other hand, gets into the brain where it is transformed into dopamine.[2] This was the first therapeutic use of L-DOPA for Parkinson's disease. A year later, a neurologist from Canada, André Barbeau, confirmed the effect of L-DOPA for Parkinson's symptoms.[3] This was the beginning step in the development of the now classical Parkinson's therapy using L-DOPA.

However, the enthusiasm for the impressive effects of LDOPA was disturbed by the relatively short period of its action. The L-DOPA injection worked for only about 15–30 minutes, too short to establish a therapeutic concept from it. The reason of this short duration was the enzyme L-DOPA decarboxylase, which degrades L-DOPA to dopamine very rapidly in the body, before a sufficient amount of it can reach the brain.

Professor Alfred Pletscher, head of research and development at Hoffman La Roche at that time (1965), offered my father a substance that he claimed was an inhibitor of L-DOPA decarboxylase. He injected this substance, Benserazide from Roche, and found that it extended the duration of the L-DOPA effect from a few minutes to half a day. But how could an inhibitor of an enzyme, which diminishes dopamine production, lead to an extension of the beneficial effect of L-DOPA? It was discovered that Benserazide cannot pass the blood-brain barrier, so it only inhibits the enzyme present outside the brain.[4] By inhibiting the transformation of LDOPA to dopamine only in the body, more L-DOPA reaches the brain, causing a longer lasting effect.

Further research about L-DOPA revealed that dopamine exhibits its action via a receptor, the sensitivity of which changes according to its environment. If only a few dopamine

molecules are present in the vicinity of the receptor, its sensitivity becomes very high. It reacts to minute amounts with an action. High concentrations of dopamine render the receptor more insensitive. This phenomenon represents a general biological feedback mechanism to protect receptors from too high a stimulus. The new combination of L-DOPA and the decarboxylase inhibitor allowed higher concentrations of L-DOPA to reach the brain, yet this increased level caused a reduced sensitivity of the dopamine receptor. As a consequence, the action of L-DOPA became weaker, particularly when patients were taking higher doses and for a longer period of time. The transmission of the signals triggering movements in the body did not function in the way wanted by the patient.

Researchers discovered substances that were capable of increasing the sensitivity of dopamine receptors, called dopamine receptor agonists. Some of these dopamine agonists have been used with Parkinsonian patients and improved their symptoms, particularly in those patients treated with relatively high doses of L-DOPA. The main drawback of dopamine receptor agonists is that certain agonists inhibit tyrosine hydroxylase, the key enzyme for the biosynthesis of L-DOPA. This enzyme is already reduced in the brains of Parkinsonian patients. If the low activity of this enzyme is further reduced by dopamine agonists, the symptoms intensify.

Dopamine is further processed by the enzyme monoamine oxidase (MAO). So, inhibiting MAO should result in an increase of dopamine in the brain. Various MAO inhibitors improved the symptoms of patients suffering from depression, yet they were ineffective for Parkinson's disease. In 1974, Joseph Knoll, professor of pharmacology at Semmelweiss University, in Budapest, developed a substance he called L-Deprenyl, which inhibited monoamine oxidase type B (MAO-B). This particular type of monoamine oxidase degrades dopamine. If L-Deprenyl was specific and effective for this enzyme, it should slow down the metabolism of dopamine in the brain and mitigate the symptoms of Parkinson's patients.

My father started to treat Parkinsonian patients with LDeprenyl and it showed remarkable beneficial effects, particularly with patients who were under long-term L-DOPA treat-

ment. Deprenyl reduced the fluctuations in the patient's condition: those receiving Deprenyl together with L-DOPA exhibited a more pronounced improvement of their symptoms. Patients lived longer when taking Deprenyl than those who received L-DOPA alone.[5] In 1981, researchers from Mount Sinai University, in New York, found that Deprenyl alone improves the symptoms of Parkinson's, particularly in the early stages of the disease.[6]

A New Approach in Parkinson's Therapy—NADH

The therapeutic concepts for Parkinson's disease discussed so far are based on the substitution of the missing dopamine by L-DOPA. This lack of dopamine arises because tyrosine hydroxylase, the enzyme that produces dopamine in the brain, exhibits greatly reduced activity in Parkinsonian patients. The co-factor of this enzyme is tetrahydrobiopterin, which is also diminished in Parkinson's patients. For the formation of tetrahydrobiopterin, the cell needs a further coenzyme, namely NADH; NADH also activates tyrosine hydroxylase. Because of these actions, studies have found that NADH increases the production of dopamine up to sixfold in cultures of nerve cells.[7]

On the basis of the actions of NADH on the biosynthesis of dopamine, I suggested to my father that he consider NADH as a new therapeutic concept for Parkinson's disease. NADH had been available in pure form for decades for use in diagnostic blood tests. Its therapeutic application, however, had never been considered, because the scientific community was convinced that NADH was too reactive and would degrade too rapidly. Personally, I was convinced that NADH would cause a positive effect and I gave my father an ampule of pure NADH. He gave the NADH (20 mg) intravenously to a Parkinson's patient who had suffered from the disease for a couple of years. The patient had difficulty getting out of his chair and could only walk in small clumsy steps. One hour after the NADH infusion, he could get up without problems and could even jump. This was in May 1987.

The logic behind this approach was to stimulate the biosynthesis of dopamine in the brain by using NADH.[8] The basic difference with the substitutional therapy using L-DOPA was the ability to stimulate the production of the lacking dopamine.

Based on the these encouraging effects of NADH, we treated many Parkinsonian patients by infusing NADH intravenously. After the first 130 patients, we concluded that NADH led to an improvement of symptoms in over 90 percent, particularly increases in mobility and energy. Also, the

phases of good mobility as well as the alleviation of depressed mood, frequently observed with Parkinson's patients, were longer lasting.[9] After treating 425 patients with NADH, these results were confirmed: in 88–90 percent of patients, mood, posture, mobility, punching force, and the articulation of speech improved.

Many of the patients asked why NADH was not available in tablet form. My father conveyed his patient's wish to me and requested that I develop NADH tablets as soon as possible. As already discussed, this turned out to be a real challenge. My father was a world-renowned Parkinson's disease specialist and received patients from all over the world for NADH infusions. However, this therapy was feasible only at our clinic, the Birkmayer Institute for Parkinson's Therapy, in Vienna. Thus, patients from abroad were frustrated that they could not receive NADH infusions at home. Furthermore, they did not want to visit a clinic every two weeks for further NADH treatment.

As soon as we had NADH tablets available, we started using it for treating Parkinsonian patients. In one year, 480 patients were treated with NADH tablets: 85 percent showed a significant improvement in the Parkinson disability rating scale (between 10 and 60 percent) after just 2–4 weeks. The improvements seen with oral NADH were comparable to those with the intravenous form. The only difference was the duration of the effect. After infusion of NADH, a beneficial effect was observed within thirty minutes, but the tablets took two hours. However, the tablets' beneficial effects were longer lasting.[10]

DEPRESSION

Depression is the general term for a deterioration of well-being, of mood and the joy of life. The economic damage caused by depressive diseases has been estimated at $40–77 billion in the United States. And depression is becoming a worldwide epidemic. The so-called “burn-out syndrome” is another term for a depression caused by physical and mental exhaustion. The main symptoms of depression are:

- Lack of enterprise
- Feelings of the futility of life
- Lack of interest
- Reduced libido
- Lack of enjoyment
- Constipation
- Lack of concentration
- General pessimism
- Reduced performance
- Self-reproach
- Loss of sleep
- Anxiety
- Loss of appetite
- Suicidal tendencies
- Low drive
- Hypochondria

Certain neurotransmitters such as adrenaline, dopamine, and serotonin play a key role as the biochemical cause in the development of depression. The level of these neurotransmitters is generally low in the brain of depressed people. Due to this, their biological functions are diminished as well. The most important functions of noradrenaline, dopamine, and serotonin are listed below.

PHYSIOLOGICAL FUNCTIONS OF NORADRENALINE	
HIGH LEVELS LEAD TO:	**LOW LEVELS LEAD TO:**
High blood pressure	Low blood pressure

High heart pulse rate	Lower pulse rate
Muscle cramps	Slack posture
Sleeplessness	Lack of initiative
Agitated behavior	Fatigue and apathy
Restlessness	

PHYSIOLOGICAL FUNCTIONS OF DOPAMINE	
HIGH LEVELS LEAD TO:	**LOW LEVELS LEAD TO:**
Involuntary choreic movements	Slow movements (hypokinesia)
Compulsive movements	Physical fatigue
Emotional hyperactivity	Leaned posture
Tonic muscle cramps	Weariness
Tendency to anorexia	

PHYSIOLOGICAL FUNCTIONS OF SEROTONIN	
HIGH LEVELS LEAD TO:	**LOW LEVELS LEAD TO:**
Elevated appetite	Sleep disturbances
Weight gain	Slack posture
Sleepiness	Inactivity
Depressed mood	Introversion
Diarrhea	
Slowing of cognitive performance	
Loss of drive	

NADH stimulates the biosynthesis of these neurotransmitters. Since depressed people have a deficit of noradrenaline, dopamine, and serotonin in the brain, it appeared a reasonable approach to treat patients suffering from depression with NADH to improve their symptoms. From 1990 to 1992, 205 depressed patients were treated with NADH at our clinic in Vienna in an open label clinical study. The patients received NADH (10 mg per day) either intravenously, intramuscularly, or in tablet form for a period of six months. At the end of the study period, 93 percent of the patients experienced an improvement of their symptoms (up to 44 percent in the depression rating scale). A number of patients observed an alleviation of their mood after only five days of NADH treatment; others improved after four weeks.[11] No side effects were reported.

In the meantime, a couple of thousand patients suffering from depression, the majority of them in the United States, have been taking NADH tablets for an even longer period of time. They all reported beneficial effects on their physical and mental exhaustion. The antidepressant effect of NADH was confirmed in a study with rats. Rats develop depressive symptoms, reflected by their obvious inactivity and their swimming abilities, which decline strongly. The “swim tests” for rats is a standardized, generally accepted way to study their depressive behavior. Using this test system, NADH led to an improvement of activity in the rats, which exhibited an increased readiness to perform the swim test.[12]

CHRONIC FATIGUE SYNDROME

Chronic fatigue syndrome (CFS) is characterized by extreme exhaustion and inability to work.[13] In Europe, CFS is better known as myalgic encephalomyelitis (ME).[14] This disease is characterized by various symptoms and complaints not necessarily related. Worldwide, a couple of hundred million people suffer from CFS.[15] The U.S. Centers for Disease Control (CDC) has defined criteria for chronic fatigue syndrome:

- Fatigue lasting six months
- Mild fever or chills
- Sore throat
- Painful lymph nodes
- Muscle weakness
- Muscle pain
- Joint pain
- Fatigue that lasts twenty-four hours after exercising
- Headaches
- Short-term memory problems (forgetfulness)
- Depression
- Sleep disturbances

These symptoms have to persist for at least six months in order to comply with the definition of CFS.[16] The CDC did not state whether all or how many of the symptoms have to be present in order to fulfill the definition. Most of the symptoms characteristic for chronic fatigue could also be caused by other chronic diseases, such as cancer, heart failure, immunodeficiency, rheumatoid arthritis, and many others. All of these diseases have to be excluded before a definitive diagnosis of chronic fatigue can be made. A variety of blood tests are required in order to find out what might be the cause of the debilitating fatigue.

Using a special method of computer tomography, scientists at a research center in the U.S. found out that patients with CFS exhibit a lower level of ATP (adenosine triphosphate) in their muscle tissue than healthy control subjects. This finding

explains the muscle weakness and the tiredness triggered by it—complaints reported by many CFS patients.[17]

Based on this report and our own observation that NADH increases ATP production in cells, a study with CFS patients was performed to investigate the efficacy of NADH for CFS symptoms. A double-blind, placebo-controlled cross-over study was performed at Georgetown University, in Washington, D.C. CFS patients received 2 tablets of NADH (a total of 10 mg) per day or a placebo for four weeks. This first treatment was followed by a four-week wash-out phase, during which neither group received tablets. Then, the NADH group received the placebo and the placebo group received the NADH tablets. The result showed that 31 percent of the patients exhibited an improvement in their symptoms after four weeks of treatment. After six months of NADH supplementation, 82 percent reported relief from their symptoms.[18] Further reports on the application and the effect of NADH with CFS have been summarized in numerous scientific journals.[19]

ALZHEIMER'S DEMENTIA

Dementia can be defined as loss of intellectual functions, such as logical thinking, calculating, reading, memory, and ability to concentrate, as well as comprehending and reacting on optical and acoustic signals, to mention just a few of them. The inability to process information and to set actions based on this, as well as to perform personal hygiene, are symptoms of cognitive impairment. The perception of the five senses seems to function properly, yet the memory, particularly the short-term form, is considerably reduced.

Recognition of a stimulus is information that should be stored in the mind, but in dementia a break lies in the process of transforming the stimulus into a message to be stored in the brain. The signal of a red light at a street crossing, the sound of a car horn, even touching the body triggers a message transmitted to certain areas in the brain. Whether or not all these signals are stored as information in the brain depends on the importance of the message. This information storage process is called memory.

Research in recent years found that different signals are stored in different areas of the brain. The memory for sensory information is laid down in the frontal part behind the forehead. The duration of storage lasts only a few seconds, and if the signal is not particularly strong it is deleted rapidly to make space available for new incoming signals. Only stimuli judged as important by the brain track their way to other areas where longer storage is programmed.

Names, news, facts, events, or earlier experiences are stored in the so-called explicit memory located in the hippocampus, an area in the central part of the brain. The storage time in the hippocampus lasts from minutes to months, depending on the importance the individual gives this information. Activities of a person performed regularly, causing some kind of automatism, are stored in the unconscious memory, also called implicit. The implicit memory is located to the greatest part in the cerebellum, the small brain. This memory functions relatively long normally in patients with dementia. A further form of storage for information is the emo-

tional memory, located in the limbic system, an area in the mid-brain.

Dementia is characterized by a variety of symptoms, which curtail the mental as well as the physical capabilities. The most frequent form of dementia is the one discovered and described by the German pathologist Alois Alzheimer in 1903. Worldwide, 5 percent of the population over sixty-five years of age is afflicted with Alzheimer's disease. In the U.S., more than 5 million people suffer from Alzheimer's dementia and the incidence is increasing. The clinical appearance of Alzheimer dementia is reflected by loss of memory, worsening of intellectual capabilities, and impairment of daily social activities. Symptoms of the disease include difficulties in learning and decline of judgment, disorientation in time and place, and loss of communication skills.

Professor Barry Reisberg, of New York University, one of the world's leading experts on Alzheimer's, has developed a global deterioration scale (GDS) for age-associated cognitive decline of patients. He distinguishes seven stages in the development of Alzheimer's dementia.

Examining Cognitive Performance

A relatively simple method to examine cognitive performance is called the Mini-Mental Status Examination (MMSE). This procedure gives a rough overview about the mental performance of the brain in less then five minutes. It can be performed by anybody.

Orientation

1. What is the year? (1 point)
2. What is the season? (1 point)
3. What is the date? (1 point)
4. What is the day of the week? (1 point)
5. What is the month? (1 point)
6. In which country are we? (1 point)
7. In which state are we? (1 point)
8. In which city? (1 point)
9. Where are we now? (1 point)
10. In which street? (1 point)

Registration

11. Examiner names three objects.
12. Examiner asks patient to repeat all three (1 point for each correct answer)

Attention and Calculation

13. Serial sevens. (1 point for each correct answer)

Alternative: spell a word with 5 letters (e.g., world) or count numbers backwards (e.g., 99 to 94). (maximum 5 points)

Recall

14. Examiner asks again for the three objects from task 11. (maximum 3 points)

Comprehension, Speech and Activity

15. Examiner points to a pencil and a watch. The patient has to name them as you point. (maximum 2 points)
16. Examiner has the patient repeat "No ifs, ands, or buts." (maximum 1 point)
17. The patient has to follow a three-stage command such as: "Take the paper in your right hand. Fold the paper in half. Put the paper on the floor." (maximum 3 points)
18. Have the patient read and obey the following: "Close your eyes." (Write in large letters.) (1 point)
19. Have the patient write a sentence of his or her own choice. (The sentence should contain a subject and an object and should make sense. Ignore spelling errors when scoring.) (1 point)
20. Examiner draws two intersected pentagons about 5 centimeters and have the patient copy it. (Give 1 point if all sides and angles are preserved and if the intersecting sides form a quadrangle.) (1 point)

The maximum score of 30 points indicates normal brain performance. If a test person reaches less the 24 points, this may be the first hint of reduced cognitive function. With this low score, the cause for the disturbance should be elucidated as it may indicate a beginning Alzheimer's dementia.

Stage 1: No subjective complaints of memory deficit.

Stage 2: Subjective complaints of memory deficit (e.g., forgetting names or numbers).

Stage 3: Family members or colleagues recognize a reduced performance.

Stage 4: Reduced capability to accomplish complex tasks (e.g., prepare dinner for guest or shopping with a shopping list).

Stage 5: Patient is disoriented to time and/or place and cannot live without a caregiver. Problems with dressing and personal hygiene.

Stage 6: Complete loss of social abilities. Patient must be washed, dressed, and accompanied to the toilet.

Stage 7: Loss of speech and psychomotor capabilities.

If a healthy person steps on the street and sees a car coming, he or she realizes the danger and steps back. An Alzheimer's patient in an advanced stage will stop and stand where he is as he does not realize the danger he is exposed to.

What Causes Alzheimer's?

A number of theories for the cause of Alzheimer's dementia, but none has yet to be confirmed. Many scientists think that deposits of degenerated brain tissue, amyloid plaques, are the cause. These plaques were discovered and described for the first time by Alois Alzheimer in 1903. However, amyloid plaques also occur in the brains of older healthy and alert people who do not suffer from dementia. Nevertheless, the plaques in the brain still represent the favorite hypothesis for many scientists and a lot of time and money is spent to verify this hypothesis. In spite of the numerous scientific papers published about these plaques, the definitive proof is still lacking.

For me, it does not appear reasonable that products that arise from destroyed nerve cells are the cause of the destruction of these cells and of brain tissue. This seems to be an illogical conclusion. Recently published scientific articles have strongly questioned amyloidal plaques as the cause for Alzheimer's. It is generally accepted by the scientific community that organs and tissues get damaged by oxidative stress. The brain is most sensitive to the attack by free radicals (reactive oxygen molecules). These destroying agents are increasingly regarded as a cause for the degeneration of the brain and the dementia triggered by it. Recently, it was discovered that brain tissue damaged by oxidative stress contains less amyloidal plaque than the intact, undamaged brain tissue. From these findings, researchers concluded that the accumulation of amyloidal plaques is an age-dependent physiological reaction but not the cause of dementia.[20]

My hypothesis for the development of Alzheimer's disease is derived from a chronic energy deficiency in the brain. How can this long-lasting lack of energy arise in the nervous system? The most logical answer is by inhibition of the biosynthesis of ATP (adenosine triphosphate), the form of energy used by cells. If the ATP concentration in a cell falls below a certain threshold, the cell dies due to lack of energy. Numerous substances have been identified that can block the production of ATP in the cell, including toxic pharmaceuticals, il-

licit drugs, alcohol, environmental toxins, and compounds derived from mercury, cadmium, or aluminum. All of these substances can trigger irreversible damage to nerve cells.

The brain is very sensitive and reacts rapidly to lack of oxygen. If the blood circulation to the brain is blocked for a few minutes, a person becomes unconscious. The longer the brain is without a blood supply, the more severe and irreversible is the functional damage. However, oxygen is only one of the two essential components needed for the energy production in a cell. The biological form of hydrogen, NADH, is the second. If the NADH content of a cell falls below a certain level, the cell is unable to produce ATP and dies due to lack of energy. NADH is the fuel for energy production in every living cell. As oxygen is ubiquitous in the body if the circulation works properly, NADH is the limiting factor in ATP production.

Without NADH, no energy production occurs in the cell. The oxygen supply for the brain is guaranteed if the blood circulation works normally, and this seems to be the case in most people, including the elderly. So, low ATP production in the brains of Alzheimer's patients must be caused by a lack of biological hydrogen (NADH). This can occur when the metabolic reactions leading to NADH biosynthesis are slowed down or blocked totally. Many compounds can reduce the metabolic pathways in our organs and, as a consequence, the cells and organs produce less NADH.

Even if a cell has sufficient amounts of NADH, this is no guarantee of sufficient ATP, because the concerted action of a number of enzymes in the mitochondria, the power plant of the cells, is necessary. If one of the various enzymes does not function properly, no ATP is formed. A number of substances inhibit these enzymes, including some of the most frequently used medicines, such as blood pressure–lowering and cholesterol-lowering drugs. One of the most important enzymes for energy production, NADH–cytochrome c–reductase, was found to be strongly reduced in the brains of the Parkinson's patients.[21] These findings support the assumption that a deficit in energy production in nerve cells is the cause of Alzheimer's.

Nerve cells are very sensitive to toxins damaging the DNA. If the brain is exposed to such compounds, the DNA repair system is activated. The enzyme system that repairs DNA needs NADH for full functionality, so the more the DNA is damaged, the more NADH is required. However, if too much NADH is used for DNA repair, very little or nothing is left for energy (ATP) production. If the ATP level in the cell falls below a critical threshold, it cannot perform its vital functions and dies.[22]

NADH for Alzheimer's Dementia

If an ATP deficit is actually the cause of Alzheimer's dementia, then using NADH as a fuel for cellular ATP production should have a positive influence on symptoms. Under this premise, a double-blind, placebo-controlled clinical trial with Alzheimer's patients was organized at Georgetown University, in Washington, D.C. Patients received 2 tablets of NADH (a total of 10 mg) per day. Seventeen patients completed the six-month study. Their cognitive capabilities were tested using the Mattis Dementia Rating Scale (MDRS) as well as part of the Cog-Screen Test battery, both commonly used measures. The MDRS showed an improvement in cognitive performance to 108.5 points after NADH, compared to 107 points at the beginning of the study; in patients taking a placebo, cognitive performance declined to 99 points. Further significant improvements were observed with the Verbal Fluency Test as well as the Fuld Object Memory Test.[23]

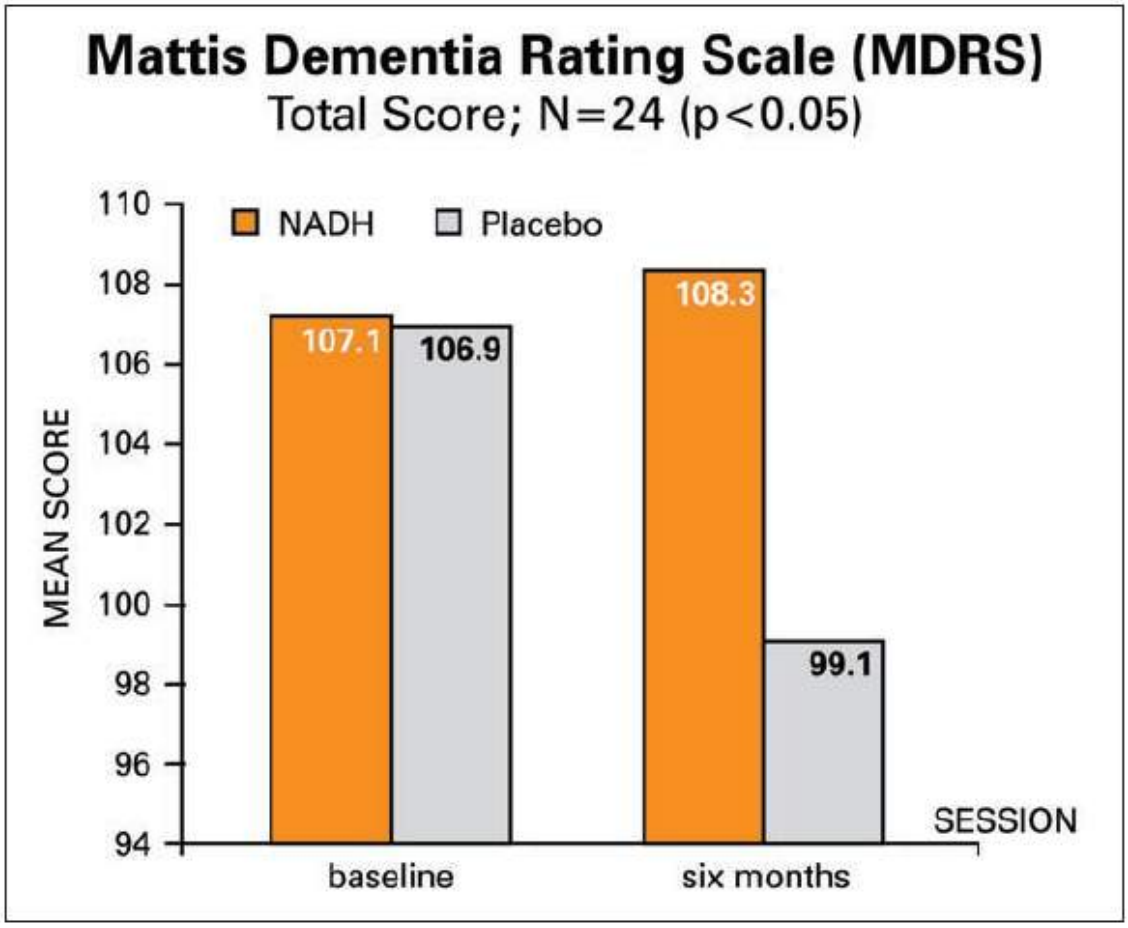

Figure 4.1. Results of the cognitive performance test, measured by the Mattis Dementia Rating Scale, of Alzheimer's patients before and six months after treatment with NADH.

Based on these promising results, a further study was done at the University of Zagreb, in Croatia. Forty-four Alzheimer's patients completed the treatment period of six months. The outcome of this study was very positive: patients treated with NADH exhibited a significant improvement in the Fuld Object Memory Test as well as in the Verbal Fluency Test. The overall cognitive performance, as measured with the MDRS, improved under NADH treatment. On the other hand, patients taking placebo for six months showed a considerable decline in all the tests performed.[24]

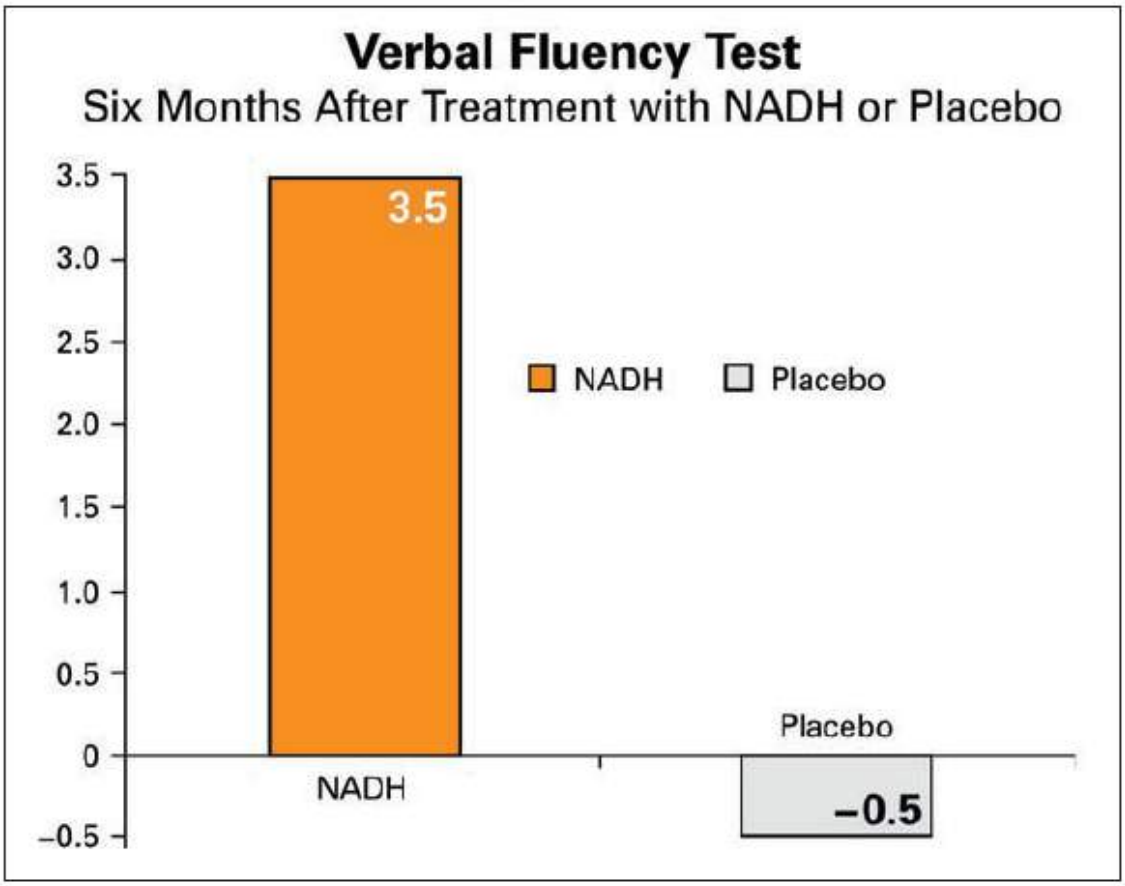

Figure 4.2. Verbal fluency test.

Based on these two independent studies, we can conclude that Alzheimer's patients improve their cognitive performance significantly after six months of treatment with NADH. NADH appears to be the first, and so far only, substance leading to improvements, because all the Alzheimer's drugs currently

available on the market only slow down the progression of the dementia.[25]

CANCER

How does cancer develop? Two phenomena appear to be the most reasonable causes:

1. Alteration of the genetic material (a mutation in the DNA).
2. A deficiency in ATP energy, leading to a lack of cellular components essential for cell regulation.

In terms of DNA mutations, there are a lot of agents able to modify the DNA. If cancer develops by the action of a substance altering the DNA, this substance is called a carcinogen. Carcinogens are frequently taken up by the human body and can induce cancer. Some medicines, such as cisplatin, also act as carcinogens. Certain compounds, not carcinogenic per se, are transposed into carcinogens in the body; these are called pro-carcinogens.

Examples of a pro-carcinogens are certain amines, such as putrescine and cadaverine, that are formed from amino acids metabolized from proteins in meat. Nitro compounds, such as nitrate or nitrite, transform these amines into nitrosamines, which are carcinogens. Nitrosamines occur in smoked, pickled, or grilled meat. We take up nitrates mainly with our daily food, as they are used as nitrogen fertilizers in the soil.

The first step in the development of a cancer cell is the binding of the carcinogen to the DNA, which causes an alteration of its structure. This modified DNA is replicated during cell division. However, cells have developed a DNA repair system, able to correct the DNA modification. If this repair system works properly and in time, the altered DNA is reverted to normal and no cancer cell will develop.

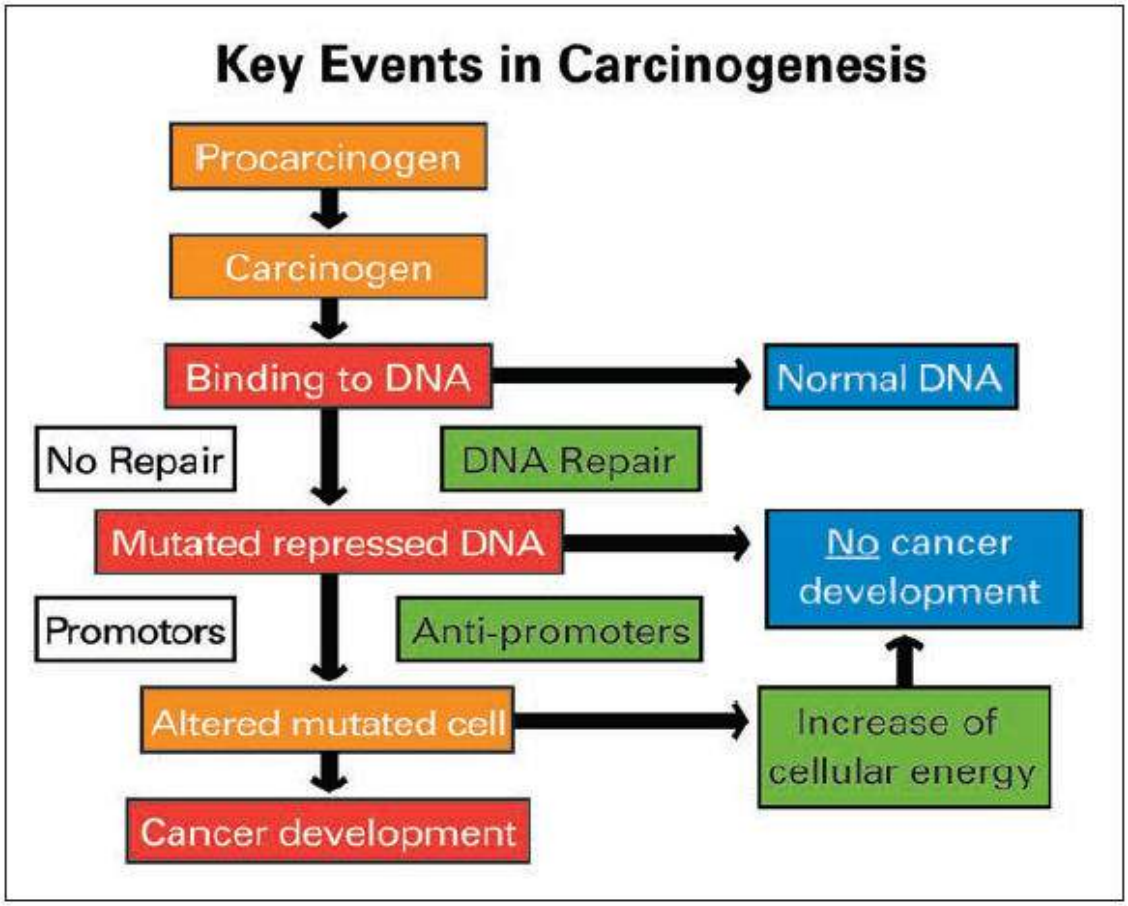

Figure 4.3. Key events in carcinogenesis.

If the mutated DNA is further modified by promoters, the probability of altered, neoplastic (cancerous) cells being formed is very high. Hence, the key in the prevention of cancer is blocking the action of promoters. Promoters are either free radicals or substances capable of producing them. The most important promoters are:

- Free radicals
- Pesticides/herbicides
- X-rays and cosmic rays
- Industrial toxins
- Ionizing radiation
- Smoking
- Nuclear radiation
- Polluted water
- UV light

- Immune-suppressive drugs
- Electromagnetic fields
- Cytostatics
- Overhead power lines
- Mercury (amalgam dental fillings)

As can be seen, there are physical and chemical promoters, both of which have the capability to produce free radicals. Free radicals are extremely reactive atoms or molecules with an unpaired electron. Due to this high reactivity, they attack nucleic acids, lipids (fats), and proteins and can change the structures of these cell components considerably. If promoters can be inactivated by anti-promoters, no cancer cell will develop.

The highest amount of free radicals arise from oxygen:

- 1–2 x 10^{22} free radicals are formed from the oxygen we breathe.
- 1–2 x 10^{21} free oxygen radicals are neutralized from the seven liters of blood in the body.
- In the average seventy years of life, we inhale seventeen tons of oxygen, from which one ton of free oxygen radicals are formed.
- In the average seventy years of our life, 10^{16} mitoses (cell divisions) occur. The human body is built up by 10^{13} to 10^{14} cells. This implies 1–10 million cell divisions per second.
- 10^{4} occurrences of oxidative DNA damage happen in every single cell. This causes from 10^{16} to 10^{18} DNA mutations.

As you can see, enormous amounts of free oxygen radicals arise in the human body just from normal processes. How can we protect the body against these aggressors? The best free radical scavengers are antioxidants, substances that act against oxidation. Naturally occurring biological antioxidants, which occur in living cells, include vitamins A, C, and E, as well as selenium, glutathione, NADH, and certain enzymes. The strength of an antioxidant depends on its capacity to prevent oxidation. The counterpart of oxidation is reduction—a substance with a high reduction power is a strong antioxidant.

NADH exhibits the strongest reduction power of all biologically occurring substances.

The alteration of mutated cells caused by the action of promoters forms the basis for the development of cancer. Another important fact is that most cancer cells contain fewer mitochondria, the power plants in the cell. Hence, these cells do not produce sufficient ATP energy for regular cell division, leading to uncontrolled and irregular cell multiplication.

The other typical behavior is the spreading of tumor cells to other organs and tissues (metastasis). This phenomenon, specific for cancer, is based to a great extent on the lack of receptors on the surface of cells. These molecules, present in normal cells, are essential for intercellular communication. Cancer cells grow rankly into healthy neighbor tissue as they do not recognize the adjacent cells due to the lack cell surface receptors. Normal cells do not show this phenomenon and sense their neighbor tissue, which signals them to stop growing into that area.

NADH for Cancer

If a deficiency of ATP is indeed the cause of cancer, supplying ATP from outside to the cells and tissues might be a reasonable approach of inhibiting the unlimited multiplication of tumor cells. How can we compensate for the ATP deficiency in cancer cells? ATP level in isolated cells can be increased by providing the cells with NADH. If these cells get more ATP by NADH, they may then be able to synthesize molecules essential for regulation of cell division. If cell division is normalized, growth of cancer cells is stopped as a consequence.

NADH functions in a threefold way as protector against cancer formation:

1. NADH is an essential factor for DNA repair.
2. NADH is the strongest biological antioxidant.
3. NADH increases ATP energy in the cell.

On the basis of these functions, I started to treat cancer patients in 2001 by giving them NADH in tablet form. Following are a sampling of case histories that outline the progress of some of my cancer patients treated with NADH.

Small-Cell Lung Cancer

In September 2001, a 48-year-old man came to my clinic in Vienna. Six months before his visit, a small-cell lung cancer was diagnosed by magnetic resonance imaging (MRI) and confirmed by biopsy. The tumor was 6–8 centimeters in size and inoperable according to the patient's doctor, a professor at the University of Amsterdam. The patient had been treated by radiation and chemotherapy, but these treatments did not show the success the patient had hoped for. The patient, married and the father of three children, was desperate: his doctor in Amsterdam had said to him: "Make your last will, you will not survive until Christmas."

I recommended that he start on NADH, 4–6 tablets (5 mg each) per day. In January 2002, four months after starting the NADH, the tumor size was reduced to 1.5 cm in diameter. In July 2002, ten months after beginning the NADH regimen, I received a report from the professor in Amsterdam of his recent MRI: "No tumor detectable." The patient remains in good health since then, which he indicates with thanks in his annual Christmas greeting to me.

Breast Cancer

A 63-year-old woman had an invasive ductile mammary carcinoma removed by surgery in August 1989. A year later, numerous metastases developed in the liver and in her bones. Despite four cycles of treatment with the CMF protocol (cisplatin, methothrexate, fluoruracil), the metastases increased in size.

Beginning in January 1990, the patient received NADH (12.5. mg by intravenous infusions) three times per week. Four weeks after the infusion therapy, she started taking 4 tablets (5 mg each) of NADH per day. After three months, a partial remission of the metastases was observed: some tumors were significantly smaller, and some had totally disappeared. The patient continued with the NADH therapy, and by the end of 1991 a further computerized tomography (CT) scan showed a marked reduction of the liver metastases and those in the bones had totally disappeared. In August 1994, all her tumor markers, established in blood tests for detecting cancer, were in the normal range and the patient was in good health.

Prostate Cancer

In 1994, I was visited by a manager of Lufthansa Airline, who showed me his medical report with a diagnosis of prostate cancer. In six out of seven biopsies, cancerous cells had been found. The patient was advised by urologist to have the prostate removed and to be treated with radiation and chemotherapy afterwards. He refused all of these therapeutic options because he had witnessed how a friend with the same type of cancer suffered from severe adverse reactions after radiation and chemotherapy and developed bone metastases in spite of treatment. His friend passed away after a year and a half in spite of this most aggressive treatment.

I recommended he take 6 tablets of NADH (5 mg each) per day. In addition, he was already taking selenium and shark cartilage. His prostate specific antigen (PSA) level (a blood marker for this type of cancer) was a very high 35 before beginning NADH therapy. The normal range for PSA is 2 to 5. Six months after starting NADH treatment, a normal PSA value was measured; neither an ultrasound nor a CT scan could detect a tumor in the prostate.

Brain Tumor

A 55-year-old businessman from Belgrade, Yugoslavia, received the diagnosis of a brain tumor the size of a tennis ball in 1997. The pathologists had diagnosed a rapidly growing glioblastoma, which is regarded as the most malignant type of brain tumor. The patient received radiotherapy, but this approach did not cause any shrinking of the tumor, so he was treated with cytostatic drugs afterwards. The chemotherapy also failed in reducing the size of the tumor.

I recommended that he take NADH (40 mg) as sublingual tablets. He obtained these supplements via a colleague of mine in Belgrade. The last message I received from my colleague in Belgrade regarding this patient, in 2003, reported that the tumor had regressed considerably to less than 1 cm in diameter. The patient does not have any symptoms or health problems and he feels well.

Stomach Cancer

In mid-December 2005, I was visited by a woman, 82, who was desperate: two weeks prior she had been diagnosed with a "big" cancer in the stomach. Biopsies had revealed an undifferentiated carcinoma of the stomach that had already spread to more than half of the gastric mucosa and had infiltrated adjacent tissue. She had anemia, most likely caused by the cancer, as well as very low readings of red blood cells and hemoglobin. The iron level was extremely low, whereas the tumor marker specific for this type of cancer was highly elevated.

The doctors at the university clinic where she had been diagnosed recommended a total resection of the stomach, yet they could not assure her of the complete removal of the tumor. Also, they were not certain whether or not there was additional tumor tissue outside the stomach or metastases in other organs. In spite of these uncertainties, the surgeons recommended the operation, claiming that the patient would have only a few weeks to live if the tumor were not surgically removed.

Instinctively, the patient refused to be operated on—she was afraid of the surgical intervention but even more afraid of her potential condition afterwards. I recommended that she start taking NADH, 6 tablets (7.5 mg each) daily, 3 tablets in the morning and 3 tablets in the early afternoon, for a total amount of 45 mg per day. At the end of March 2006, the patient looked much better and reported having more energy, was eating with more appetite, and was able to go shopping again regularly, which she was unable to do in December. In addition, her depressive mood, most likely triggered by the diagnosis of cancer, was gone. Three months later, all her blood readings (red blood cells, hemoglobin, iron, and the tumor marker), which had been severely altered at the time of the diagnosis, were in the normal range. Objectively, the patient left the impression of a healthy and happy person.

A new aspect of NADH action is derived from the research of Professor Isaiah Fidler, a leading expert in cancer metastasis. Dr. Fidler provides evidence that tumor cells do not metastasize if the enzyme nitric oxide (NO)–synthetase ex-

hibits full functionality.[26] Cancer cells with a reduced or altered NO-synthetase spread to other organs and tissues. Based on his observation, one could assume activation of the diminished NO-synthetase enzyme would change the metastasizing features of cancer cells to nonmetastasizing ones. An enzyme can be activated by its specific coenzyme, and the coenzyme for the NO-synthetase is NADH. NADH stimulates NO synthesis in a dosage-dependent manner by more then ten times. Due to this effect, NADH should exhibit an "anti-metastasizing" action. Dr. Fidler reports that tumor cells stop growing (cytostasis) and undergo cell lysis (cytolysis) the more NO (nitric oxide) the cancer cell produces. The more NADH a cancer cell has available, the more NO it can synthesize. Nitric oxide will then dissolve the cells of the cancerous tissue.

The regression of metastases with the patients described previously may be caused by the stimulatory effect on NO-synthetase by NADH. Patients who have been diagnosed with cancer should therefore start taking NADH as soon as possible to prevent metastases at an early state of their cancer.

STROKE

People developing a stroke exhibit impairments in their mobility, speech, or cognitive performance. If the stroke causes paralysis of one side of the body, relatives and caregivers recognize this immediately as a stroke. Triggers for a stroke could be a rupture of, or blockage in, a blood vessel in the brain. If the blood supply for a certain brain area is reduced, the brain is lacking oxygen and nutrients. No nutrients also means no NADH and hence no fuel for ATP energy production in this brain area. Without energy, the tissue gets damaged and will die. When this happens, the functions controlled by this particular brain area desist. Depending on which part of the brain, left or right side, is afflicted, the contralateral side of the body shows the symptoms of hemiplegia (paralysis) or aphasia (impairment of the ability to use or understand words). In many cases, difficulties in speech and alterations in the sensitivity of the body are the first hints of a developing stroke.

As explained previously, NADH can increase ATP energy production in cells. If one supplies the brain with NADH, the tissue damaged but not yet dead should be able to produce more ATP energy and regenerate its functions. After a while, this brain area could potentially become vital again and able to carry out its physiological functions. Depending on the size of the stroke area, the regeneration may take a few days or some months. Because NADH elevates cellular energy, I have treated a number of stroke patients by recommending they use NADH. The course of the stroke has shown remarkable benefits under NADH treatment in several cases.

- In one case, an 84-year-old woman who had suffered a stroke in June 2003 developed hemiplegia and motoric aphasia. Two weeks after the stroke, she started taking NADH, 4 tablets (40 mg) per day. After two weeks, she could get up from bed, walk, and speak. In fact, she was considerably better physically as well as mentally than she had been a month before the stroke. She continues to take NADH daily.

- In a second case, a 66-year-old man suffered a stroke in May 2003. He was confined to a wheelchair and suffered from hemiplegia and hemiparesis. He started taking NADH, 4 tablets (40 mg) per day. Two weeks later, he could get out of the wheel-chair and walk without the help of a walker. He is still taking NADH and is further improving in terms of mobility and mental ability.
- Another male stroke patient, age 39, had a complete block of the left carotid artery and, as a consequence, a severe hemiplegia. He could not lift his right hand, shake hands, or move his fingers. He started taking NADH, 4 tablets (40 mg) per day. After one month, he could lift his arm above the shoulder and could also walk considerably better. After two months, he could lift both hands above his head and was able to type on his computer keyboard with both hands. He continues to take NADH and is gradually improving even more.

The symptoms of a stroke can be improved even years after the event. Obviously, a certain part of the infarct area in the brain must not be totally dead but rather inactive and non-functional as a consequence of a low blood supply. The tissue could not be repaired and rendered functional if the brain tissue was non-vital. By supplying NADH, the cells obtain more hydrogen and can produce more of the lacking ATP energy. This additional energy allows the cells to regenerate and restore compounds essential for their full functionality.

The positive effects of NADH with stroke patients and the mechanism of its action has been noticed by neurologists. A study is planned at a neurological clinic in Germany to confirm the efficacy of NADH in stroke patients.

DIABETES

Diabetes is characterized by a constantly elevated blood sugar value. There are two main types of diabetes:

- Type 1 is insulin-dependent diabetes, also called juvenile diabetes.
- Type 2 is non-insulin-dependent diabetes.

The reason for the elevated blood sugar is a lack of insulin. This hormone exhibits a variety of biological effects. It promotes the uptake of sugar (glucose), amino acids, and fatty acids into the cell. It also inhibits the degradation of glycogen, the "sugar pool" of our body, as well as that of proteins and fats. Insulin triggers the transportation of glucose from the blood into the cells. which is urgently needed as the cell needs to make NADH out of glucose. NADH, as fuel for energy production in the cell, will then generate ATP. If the organism suffers from an insulin deficiency, less glucose is transported into the cells and the sugar level in the blood increases.

Diabetic patients, due to their insulin deficiency, do not get sufficient amounts of glucose into their cells. Hence, these cells produce less ATP energy than cells from healthy individuals. As a consequence, they cannot synthesize components in the amount required to fulfill all the specific functions of the cells and the tissue. The beta-cells of the pancreas are specialized to produce insulin. If these cells are lacking ATP, they are unable to produce normal amounts of insulin and the deficiency of this hormone triggers diabetes.

According to new research findings, it appears that type 2 diabetes is caused by faulty function of the mitochondria, the power plants of the cell.[27] If the mitochondria are damaged, energy production in the cell declines. This also happens in the beta-cells of the pancreas, which then produce less or no insulin. Numerous factors are regarded as cause for the dysfunction of mitochondria with type 2 diabetes, particularly elevated cholesterol and triglyceride concentrations in the blood. However, cholesterol-lowering drugs can also induce damage in the function of mitochondria.

Cholesterol is the basic substance from which many hormones, including sex hormones, are synthesized in the body. This holds also for coenzyme Q_{10} (CoQ_{10}), which plays an important role in energy production in the mitochondria. If the biosynthesis of cholesterol is blocked, ATP production declines. In the beta-cells of the pancreas, this would mean that no insulin could be synthesized due to the lack of energy. Diabetes is the consequence. If we can increase the ATP level in these cells, insulin production may be restored. A few years ago, scientists showed that insulin production in the pancreas can be stimulated by ATP. They rinsed an isolated pancreas with an ATP-containing solution and observed an increased ATP production.

The first anecdotal reports of a normalization of elevated blood sugar after application of NADH were received in the early 1990s. When my father gave NADH to Parkinson's patients who were also afflicted by type 2 diabetes, they achieved normal blood sugar levels after 3–4 weeks; they were unable to reach this using their normal anti-diabetic medication.

NADH tablets have been taken by many people on a regular basis and I have received feedback from a number of them about the normalization of their blood sugar levels. A colleague of mine has been treating type 2 diabetic patients with NADH in his clinic in the U.S., and many of his diabetic patients are now taking only NADH tablets in lieu of their standard anti-diabetic medication. A number of type 1 diabetic patients needed a lower daily insulin dose when taking NADH regularly. Controlled clinical studies are also in progress to confirm the anti-diabetic effects of NADH.

A further observation is worth mentioning regarding the lipid-lowering action of NADH. Two men in their early forties, who were in general good health, had normal blood readings with one exception: their lipids (triglycerides) were extremely high at 500 units. Both patients mentioned they had these high values for a number of years and had been taking lipid-lowering medications for a long time. But they were ineffective in lowering their high triglyceride values. Both patients started taking NADH. After four weeks, their blood readings showed a drop from over 500 to 170 and 140, respectively.

How does NADH lower blood lipids, particularly triglycerides? I have an explanation for this unexpected effect of NADH. The level of triglycerides in the blood is elevated if the enzymes metabolizing these lipids, the lipases, are not produced in sufficient amounts. Lipases are produced from the pancreas and then secreted to the intestinal tract. There they cleave the lipids into smaller molecules to be taken up by the cells. If the pancreas does not produce enough levels of lipases, the triglycerides cannot be degraded and their level in the blood increases.

With type 2 diabetes, insulin is still produced by the pancreas, but in levels too low as this organ does not have a sufficient supply of ATP energy. What holds for the hormone insulin seems to hold also for lipases—if the pancreas obtains more ATP energy by giving the patient NADH, it will be able to produce sufficient amounts of lipases, which will degrade the triglycerides and normalize their concentration in the blood.

CHAPTER 5

Additional Therapeutic Uses for NADH

MENOPAUSE

Menopause is a natural change of life for women, a transition from a fertile to an infertile individual. During this time, the production of the sex hormones in the reproductive glands declines. The biological functions of the ovaries last only over a certain period of time in which they produce a follicle every four weeks. This tissue matures and produces estrogen, the key female hormone. The formation of this hormone drops during menopause and the drop in estrogen levels may cause some or all of the following complaints:

- Hot flashes
- Mood swings and irritability
- Profuse sweating
- Nervousness and anxiety
- Sleep disturbances
- Loss of sex drive
- Dizziness

The classic therapy for menopause symptoms is substitution of the estrogen deficiency using synthetic sex hormones. Hormone replacement therapy (HRT) has been used for decades and has been shown to improve the condition and well-being of women experiencing menopause. However, HRT has come under increased scrutiny as retrospective analyses revealed that women taking HRT regularly had a significantly higher incidence of breast cancer than those refraining from it.[1]

A study partially financed by Wyeth Pharmaceuticals (producer of the synthetic estrogen compound Premarin) and the American Cancer Society found that there was a strong link between breast cancer and hormone replacement therapy. The researchers followed 37,000 women for eleven

years. Women who had been on HRT for five years or less had as much as an 80 percent greater chance of getting breast cancer than those who had not taken synthetic hormones. Women who had been on HRT for longer than five years had 165 percent greater chance of getting breast cancer. But, researchers added, the type of breast cancer usually caused by HRT has a better chance of being cured than other types of breast cancer. That's not saying much, however. The fact remains that curing breast cancer usually involves a mastectomy and long bouts of chemotherapy and radiation therapy. And even in view of the fact that there are more cancer survivors today than in past years, estimates say that 40,000–90,000 women die of breast cancer annually.

Knowledge of this link is nothing new. Researchers in the 1930s had known that injecting rats with estrogen caused them to get breast cancer. (This study was repeated in Canada in 1960 with the same results.) What is new is that the American Cancer Society is admitting the link, even though they are trying to underplay it at the same time. There are currently about 9 million women taking Premarin, but perhaps it's time for those women on HRT to re-think their strategy. There are safer and more natural options available that protect against breast cancer while relieving the symptoms of menopause. One of these is tofu. Soy is one of the most natural ways of obtaining estrogen. Another is progesterone cream, which is found in health food stores.

The production of most hormones is regulated by a feedback mechanism, meaning the body stops producing its own hormones if it receives hormones from outside. Thus, the ovaries cease their estrogen and progesterone production if the woman is using HRT. But why do the ovaries terminate hormone production during aging? The answer appears simple: the hormone-producing cells lack ATP, the energy in the cells, needed for making hormones. My approach for treatment of menopause symptoms is derived from the assumption that an energy deficiency in the ovaries triggers a hormone deficiency. As NADH increases ATP energy production in the cells of the body, this co-enzyme should induce an increase in hormone production in the ovaries and, due to this effect, mitigate the common complaints of menopause.

Based on these considerations, a clinical study was performed in Austria and Switzerland involving forty-nine women, 45–65 years of age, who had stopped taking HRT or phytohormones for at least a month and who had symptoms of menopause (hot flashes, fatigue, sleep disturbances, and mood swings). They were given NADH (10 mg per day) for three months. All of them showed relief from their menopause symptoms.[2]

A further smaller study was performed by a gynecologists in Austria and involved fourteen women, all over forty years old, exhibiting menopause symptoms. They were given NADH for one month. All reported beneficial effects: improved libido, better memory, more energy, improved mood, less “burn out syndrome,” and fewer feelings of depression.[3]

NADH has been shown to improve menopause symptoms such as depressive mood, nervousness, sleeping disturbances, and low sex drive.[4] Phytohormones are substances that occur in plants which have a chemical structure similar to the female hormone estrogen. The most important of these are isoflavones in soy and red clover called genistein and daidzein. Isoflavones isolated from soy exhibit beneficial effects on hot flashes and sweating, and they also act positively on fat metabolism and bone density.[5] Considering these beneficial effects, it appeared reasonable to combine these two substances to achieve a synergistic effect. The combination product of NADH and isoflavones has been given to a number of women at the beginning of menopause, and all of them experienced a positive effect.

OBESITY

Obesity increases the risk for a number of diseases, such as diabetes and heart disease. It is becoming a major problem, particularly in industrialized countries such as the United States. With 66 percent of the population considered over-weight, the U.S. is top ranked. The emerging public health costs of this epidemic are estimated at $90 billion per year for the U.S. alone. Reducing the percentage of obese people could save billions of dollars in health-care costs.

How could this be accomplished? One approach might be the regular consumption of NADH as a food supplement. NADH is produced in our body from food: carbohydrates, proteins, and fat are converted to sugar (glucose), amino acids, and fatty acids, and then these small molecules are further metabolized. The hydrogen atoms present in glucose are transferred to the coenzyme NAD, a reaction that leads to NADH formation. From there, it is distributed to all organs and tissues. NADH enters the cell and produces ATP energy.

If we assume that the biosynthesis of NADH is regulated by a feedback mechanism similar to hormone regulation, then the metabolism of glucose to NADH may be reduced if NADH is supplied directly via a supplement. Since glucose is not needed for NADH production, the demand for carbohydrates would then decline. If the body takes up less carbohydrates, weight loss is the consequence. This theoretical scenario seems to actually occur in practical terms. First reports received from some of my over-weight patients indicated a reduced appetite and subsequent weight loss after taking NADH orally for a couple of weeks.

Based on these anecdotal observations, we performed a retrospective meta-analysis of the effects of NADH with chronic fatigue syndrome (CFS) patients. We evaluated the body weight of the CFS patients before and after the NADH treatment period. The outcome was a significant: an average weight reduction of 2.5 kilograms (5 pounds) in just four weeks of taking NADH (a daily dose of 10 mg).[6] This weight-reducing effect has also been observed from customers of Weight Watchers.[7]

Weight gain is caused by a simple formula: an overweight person takes in high amounts of calories and does not use them up sufficiently. The surplus in calories is stored as fat tissue in the body. Corpulent people have no energy and hence no motivation for moving and physical exercise, the only means to burn off the excessive calories By taking NADH, obese people could reduce their excessive pounds as they get more energy from NADH. Due to this energy boost, they may become physically and mentally motivated to start an exercise program or at least get more daily activity. This approach would be a natural and healthy way to lose weight and reduce the risk for a number of devastating and costly diseases.

JET LAG

Jet lag is a constellation of symptoms that occur after flying across time zones. The symptoms include general malaise and fatigue, disrupted sleep, gastrointestinal distress, and impaired cognitive performance. It affects not only pilots and flight-crew members but a large number of frequent travelers. Jet lag can degrade decision-making and communication abilities as well as memory by 30–70 percent. The disruption of the body's entrainment of the internal 24-hour cycle of temperature, sleep initiation, and other activities to the daylight cycle is believed to be the trigger for jet lag. The enormous increase in frequency of long-distance flights has increased the number of jet lag sufferers. Particularly in people who travel frequently by air, the cortisone level in the body rises considerably. High cortisone values can lead to deficits in spatial cognition and memory.

Until recently, therapeutic approaches for jet lag focused on the adaptation of the sleep rhythm to the new time zone by light therapy, stimulants like caffeine, or sleeping pills. Each of these methods has been found to lead to potential adverse side effects or is considered impractical. A new concept for alleviating symptoms of jet lag is to provide people with more physical and mental energy during the time of adaptation to the new time zone. This can be achieved by taking NADH.

The effect of NADH as a countermeasure for jet lag was investigated in a double-blind, placebo-controlled cross-over study at Georgetown University, in Washington, D.C. Thirty-six healthy women and men participated in this study. They were flown from the West coast (San Diego, California) overnight to the East coast (Washington, D.C.) with a stopover in Phoenix, Arizona, on regular commercial airline flights. The condition and the cognitive performance of the subjects were examined by performing certain tasks of the CogScreen test battery, a validated method used by the American Association of Airline Pilots and NASA

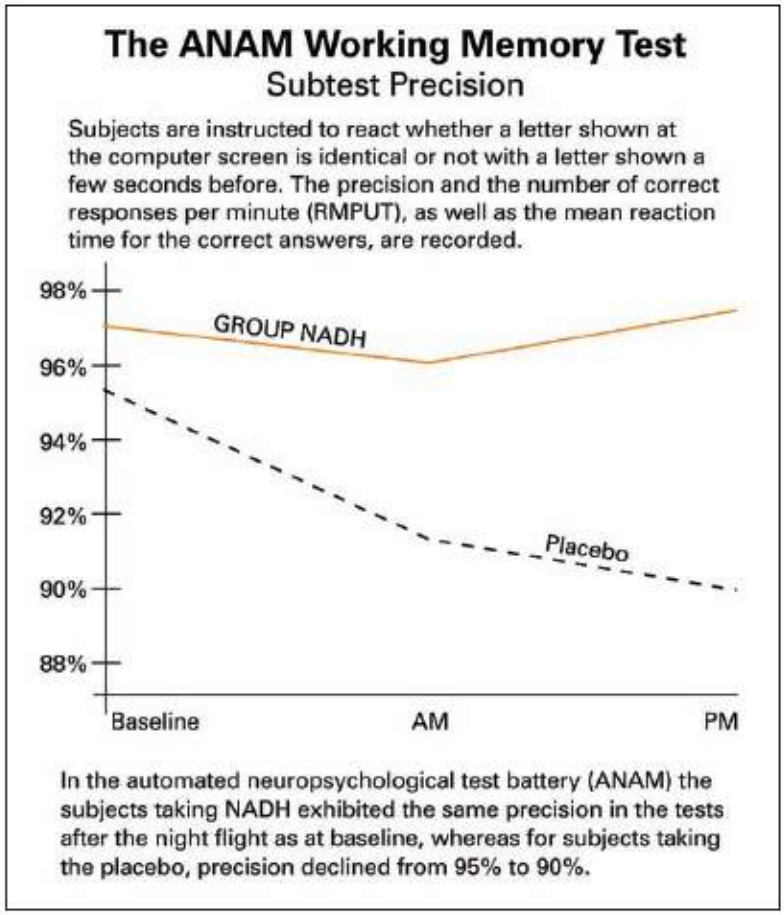

Figure 5.1. ANAM working memory test.

Two hours before departure, the subjects performed the first tests on the computer. They were each given a laptop to use over the entire testing period. The result of the first test was taken as baseline to which to compare all further test results. The subjects were flown overnight via Phoenix to Baltimore, Maryland, arriving at 6 A.M. the next day. After breakfast, they were transported to Washington by bus. One group received NADH (taken sublingually in lozenge form) and the other group took a placebo. Ninety minutes after taking NADH (9 A.M.), the subjects repeated the same computer tests; then, three hours later (at noon), the computer tests were taken again.

The study found that jet lag led to an increased sleepiness and to a deterioration of certain cognitive functions. The most frequent errors were made in concentration tests, memory tests, and the speed of visual perception (reaction time after seeing distinct signals or objects). Subjects taking NADH lozenges showed significantly better test results in terms of

cognitive performance and sleepiness than subjects taking placebo.[8]

The subjects taking NADH in the morning after the night flight exhibited the same results at the 9 A.M. test as the evening before (baseline), while those taking the placebo had much lower scores compared to the baseline. At the next test time (noon), subjects taking NADH performed even better than at baseline before departure; scores of the subjects taking the placebo declined further at the second test time. The results of this study provide scientific evidence that NADH taken sublingually improves cognitive performance after a night flight compared to the test results before departure.

SLEEP DISORDERS

As NADH can alleviate symptoms of jet lag, the question was raised whether or not NADH has an effect on symptoms of sleep deficiency. Researchers at Cornell University, in New York, conducted a double-blind, placebo-controlled study to prove the efficacy of NADH lozenges on cognitive performance impaired by sleep deprivation. Participants were kept awake for twenty-four hours. The study group was given NADH (20 mg), while the other group received a placebo.

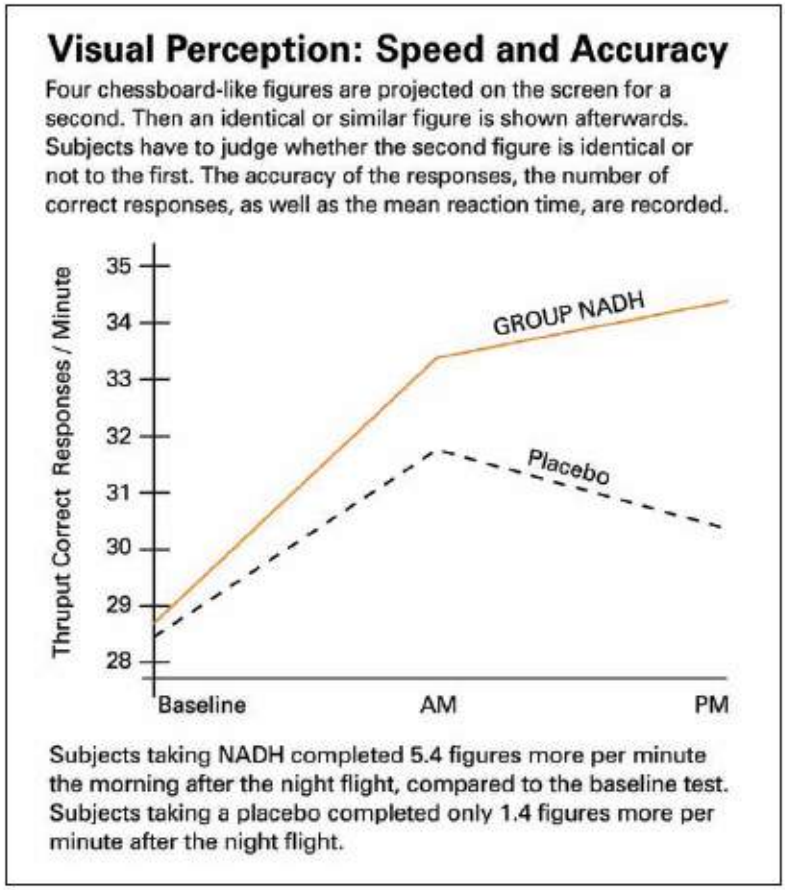

Figure 5.2. Visual perception speed and accuracy.

For this sleep deprivation study, the CogScreen test battery was used, particularly the subtest for determination of visual perception, mathematical task solution skills, and reaction time test. The beneficial effects of NADH on these capabilities after twenty-four hours of sleep deprivation were apparent:

- Total problem-solving skill was significantly better with NADH.

- Visual perception was better with NADH, both in total and in terms of speed.

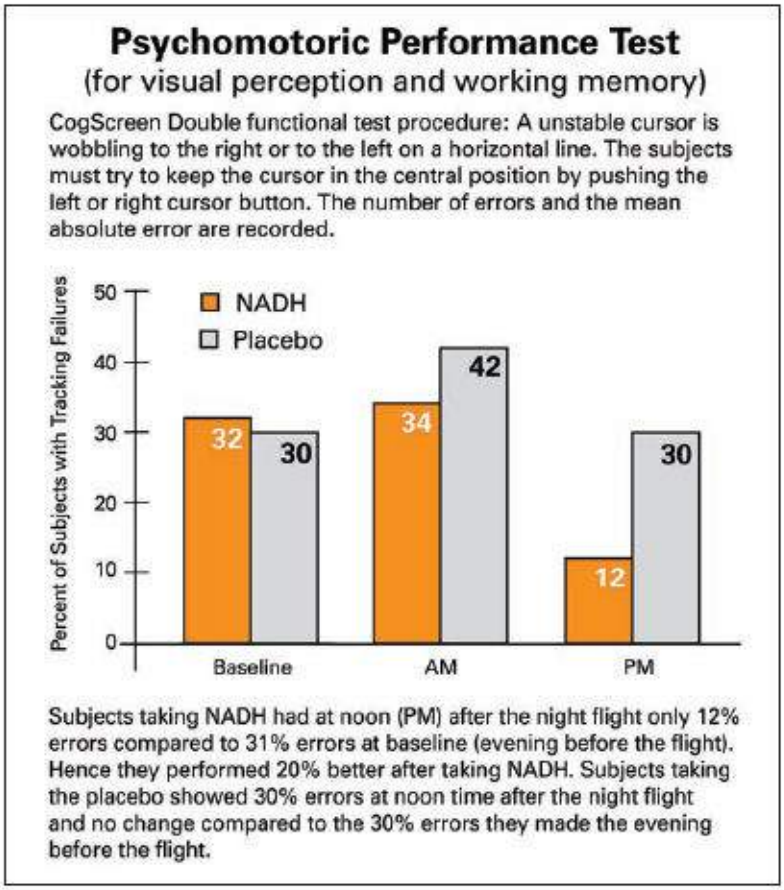

Figure 5.3. Psychomotoric performance test.

- Mathematical problem-solving was better under NADH (better even than after a full night's sleep).

The results of the study were impressive. If one does not sleep for twenty-four hours and then takes NADH, the brain functions almost four times better than after a full night of sleep without taking NADH.[9] Imagine, how much the cognitive performance may improve if one takes an NADH lozenge every morning after a full night of sleep. The study at Cornell University substantiated that NADH could improve cognitive performance that was impaired in people suffering from sleep deprivation.

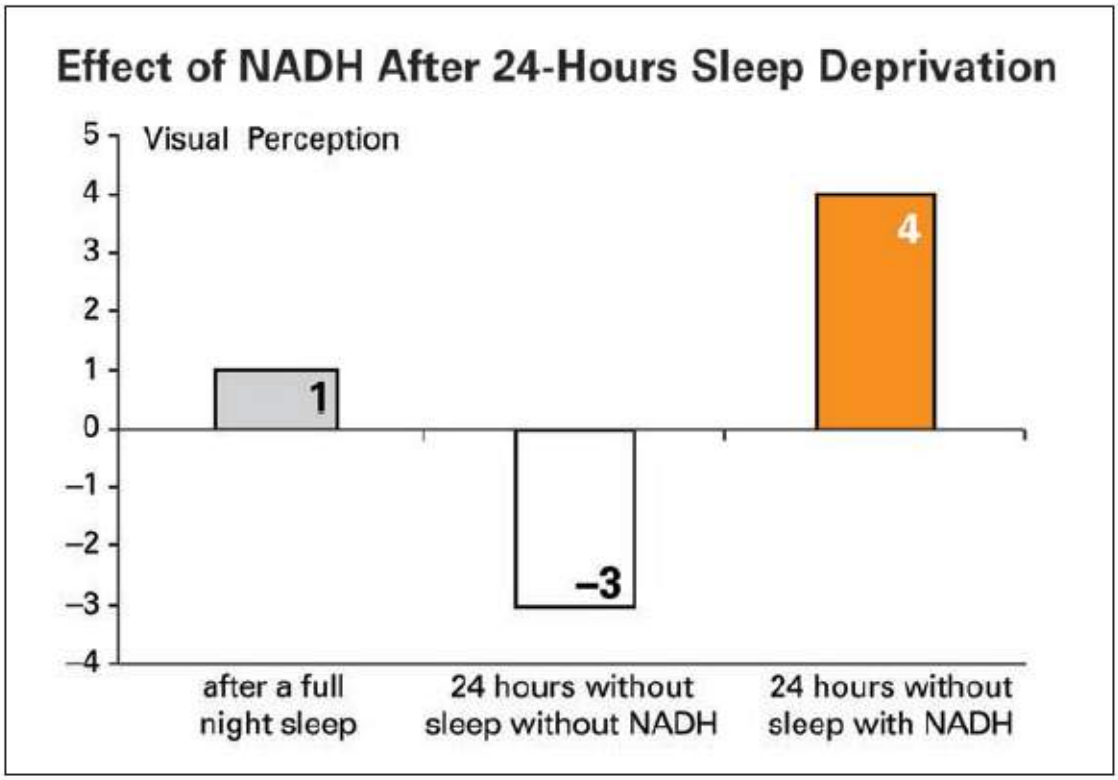

Figure 5.4. Effect of NADH after sleep deprivation.

Many readers may have experienced periods of sleep deficit and deprivation and the physical and mental fatigue triggered by it. But is it possible to measure tiredness objectively? Can a scientific method tell us whether we are tired or awake and fit? Yes, we can measure fatigue reliably and objectively. A high-tech instrument called a pupillograph measures the reaction time of the pupil in the eye. The principle is rather simple: if we get tired, the reaction of the pupil slows down. So, the contraction time of the pupil can be taken as objective parameter for fatigue.

In a pupillograph, an infrared light ray (which is harmless to the eye) is projected to the pupil in short intervals (twenty-five times per second). The pupil is dilated at the beginning of the test, as it is conducted in the dark. Each time the infrared ray hits the pupil, the pupil contracts, and this contraction is measured by a special camera. The testing time is about 10 minutes, during which the pupil receives 15,000 infrared impulses triggering the same number of reactions. From these thousands of measurements, the mean reaction time is calculated, which represents the degree of tiredness or vigilance.

The results (see Figure 5.5 below) show the reaction time of the pupil of one of my co-workers at 5 P.M., at the end of a full day of work. The reaction time (arrow in the upper part of the chart) indicates that it is lower than it should be. One hour after taking NADH (sublingually in lozenge form), the reaction time returns to normal (arrow in the lower part of the figure).

In my clinic, we used the pupillograph to prove the energizing and activating effect of NADH. Sixteen healthy subjects, 20–40 years of age, participated in the study. The first measurement was performed at 5 P.M., at the end of office hours. For the majority of the subjects, the test values indicated that they were tired after a full day of work. After the baseline test, these people took NADH (one lozenge of 10 mg). An hour later, a second measurement with the pupillograph was conducted and all participants showed a considerable improvement in their reaction time, reflecting more energy and a better vigilance. These findings confirmed previous findings that NADH has a real energizing effect and can eliminate fatigue.

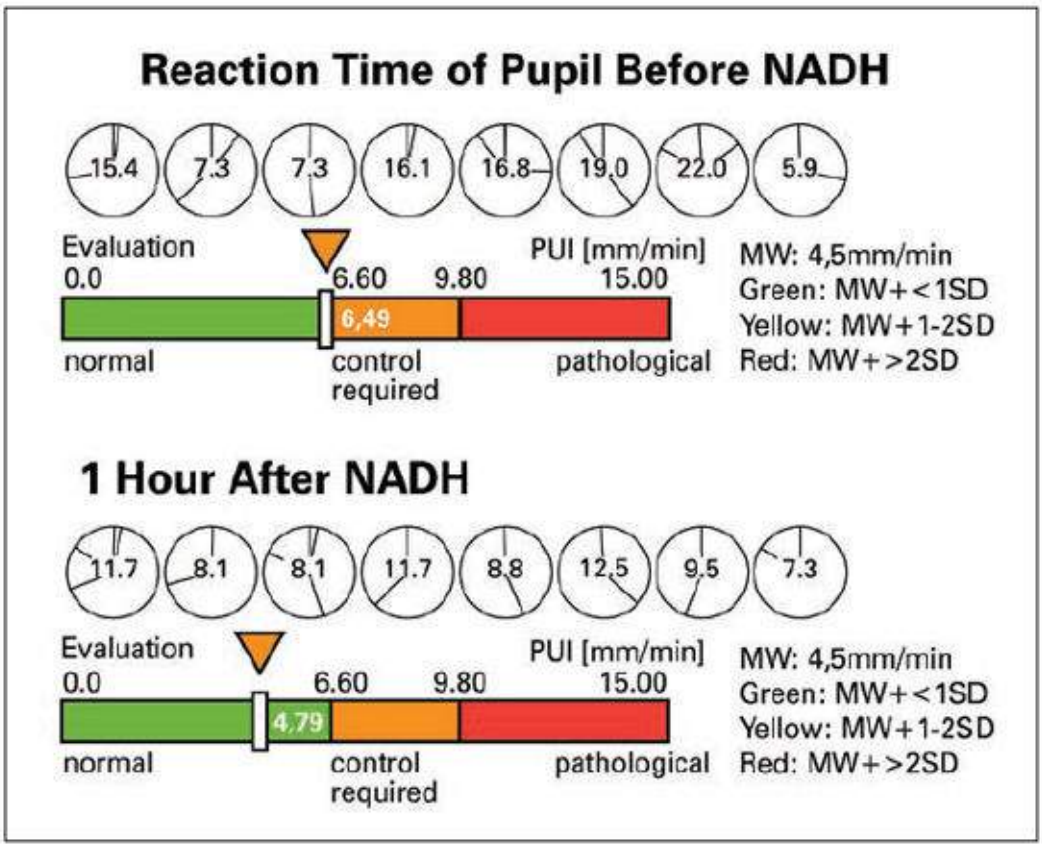

Figure 5.5. Computer evaluation of the pupillograph test results for NADH.

This anti-fatigue effect of NADH is of enormous economic importance: shift workers, doctors, nurses, as well as truck drivers are at high risk of making errors when overtired. NADH may help this group of people stay awake and work with full concentration during their night shift.

NADH IMPROVES PHYSICAL PERFORMANCE

In collaboration with a university in the Czech Republic, a study was conducted among competitive-level cyclists. They took 10 mg of NADH per day, and performance-specific parameters—vital capacity, oxygen uptake, lactate levels in blood, and reaction time—were measured before and after one month of NADH intake. It was found that oxygen uptake was faster and greater, lactate levels fell, and reaction time was significantly shorter than at the beginning of the study.[10]

A further study was performed by Dr. Bill Misner, the coach of some top U.S. athletes. He gave them NADH in a dose of 10 mg per day for sixty days. All athletes improved in their sprint performance (cycling for 5 minutes or running 1 mile), and in duration performance all the athletes also showed better values.

To confirm these preliminary findings, a study was conducted by the department of sports medicine at the University of Freiburg, in Germany. The study was a double-blind, placebo-controlled, cross-over study organized in the following way. One group of highly conditioned athletes took NADH (3 tablets, 10 mg each, per day) for four weeks. This was followed by a six-week washout period. After this resting phase, the athletes received placebo tablets for four weeks. The second group started with placebo tablets for the first four weeks, and then continued with the NADH tablets for four weeks after the six-week washout period. The following parameters were investigated: maximum aerobic capacity, oxygen uptake, carbon dioxide exhalation, lactate levels in blood, and catecholamine levels in blood. Tests were performed at the beginning and at the end of each treatment period.

After NADH supplementation, the following effects were observed:

- In the metabolic energetic area, oxygen consumption was reduced and there was an increase in the respirator coefficient.
- The exhalation of carbon dioxide was diminished as was the lactate level.[11] The lactate-lowering effect of NADH has enormous practical consequences for athletes. By taking

NADH regularly, they could theoretically exercise much longer under aerobic conditions in the muscles, leading to greater exercise duration.

- In the metabolic-regulative domain, a reduction of potassium level was observed. This could be explained by the higher demand through the defined exercise work.
- The plasma concentration of creatine was also lower with NADH. During endurance exercise, activity of the enzyme creatine kinase (CK) is higher than in the resting state. This increase is caused by leaky muscle tissue damaged by excessive use of the muscles during training. Under NADH treatment, the elevation of CK activity is much smaller than without NADH. This may be indirect evidence for the protective effect of NADH against cell damage.
- Among indicators for systemic stress, a decline of the "stress" hormones noradrenaline and adrenocorticotropic hormone (ACTH) was seen.

The reduction of the time for oxygen uptake by cells after NADH indicates an improved utilization of oxygen, which points to a higher availability of NADH and, due to this, a greater ATP level in the cells.[12] The increase of ATP in the cells was about 7 percent on average. In conjunction with the lower lactate levels, this means that the athletes can exercise for a longer period of time in the aerobic phase. This leads to better endurance and performance, particularly for marathon runners.

Researchers at the University of Jyvaskyla, in Finland, also examined the efficacy of NADH in improving physical performance in a placebo-controlled study. The results confirmed the findings of the University of Freiburg study. The lactate level in the blood, measured after an aerobic running test, was significantly lower after intake of NADH than after the placebo. Also, the jumping force was higher and the reaction times were faster after taking NADH.[13]

Some readers may be wondering: Is NADH doping? We sent this question to the medical and scientific director of the IOC (International Olympic Committee), and the answer was

concise and clear: “NADH is not on the list of prohibited substances.”

In the research department of our institute, we developed a blood test by which we can examine the energizing effect of NADH. NADH is added to a drop of blood in a test tube, and the blood cells take up the NADH immediately. Depending on the ATP pool present in these blood cells, they metabolize a lot of or little amounts of NADH. If the blood cells contain high amounts of ATP, then little NADH is metabolized and converted to ATP by the blood cells. If the ATP reserve of the cells is low, then a lot of NADH is metabolized and used for ATP production.[14]

Marathon runners before a race have a high ATP energy level, so their blood cells consume very little NADH for ATP production. After the race, the athletes have a very low energy level, and the blood test performed after the race shows a strongly increased consumption of NADH. Using this blood test, we examined the effect of NADH on the energy level of marathon runners. Athletes taking 30 mg NADH per day for four weeks showed a significantly lower consumption of NADH, corresponding to a higher ATP energy level than the athletes taking placebo. This effect was observed in all phases of the race (in the morning, after warm-ups, after the race, and then 24 hours after the race.

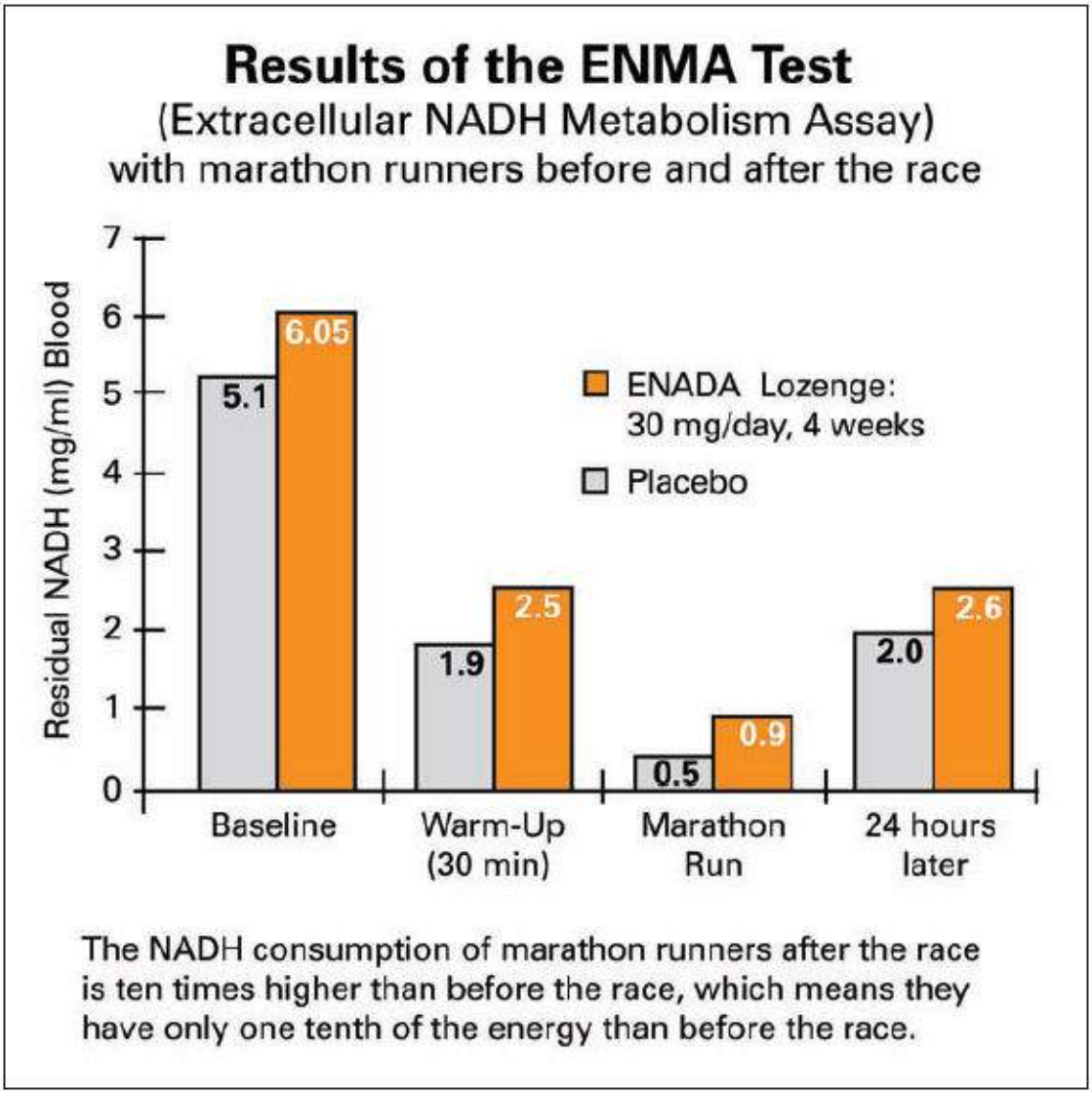

Figure 5.6. ENMA Test.

NADH BOOSTS CONCENTRATION

The number of students afflicted by a decline and impairment of their attention has risen dramatically in the last decade. The ability to focus on a certain subject for a longer period of time in class has vanished, to the distress of many teachers. This impairment is now referred to as attention deficit/hyperactivity disorder (ADHD). It is related to adrenaline and dopamine pools in the brain—if levels of these hormones are exhausted, reduced attention is the consequence.

What may be the cause of this disorder? Personally, I think a deficiency in adrenaline, dopamine, and acetylcholine is triggering this impairment, as these neurotransmitters are essential components for the cognitive performance, including vigilance, fast thinking, and short reaction time. A deficit may be because either too little of a substance is produced or too much is consumed. With ADHD, both reasons may play a role. If an energy deficiency is present in the brain, the neurotransmitters are not synthesized in sufficient amounts.

As pointed out already, the body needs NADH and oxygen for the production of ATP energy. Even if the brain has sufficient amounts of NADH available, an oxygen deficiency could lead to a lack of energy. Hence, a sufficient supply of oxygen for the cells (and particularly for the cells in the brain) is an essential prerequisite for adequate energy production. Oxygen is supplied by the blood, driven by the circulation. A reduced blood flow in the brain leads to a lack of oxygen in the nerve cells. This seems to be the case with those exhibiting symptoms of ADHD.

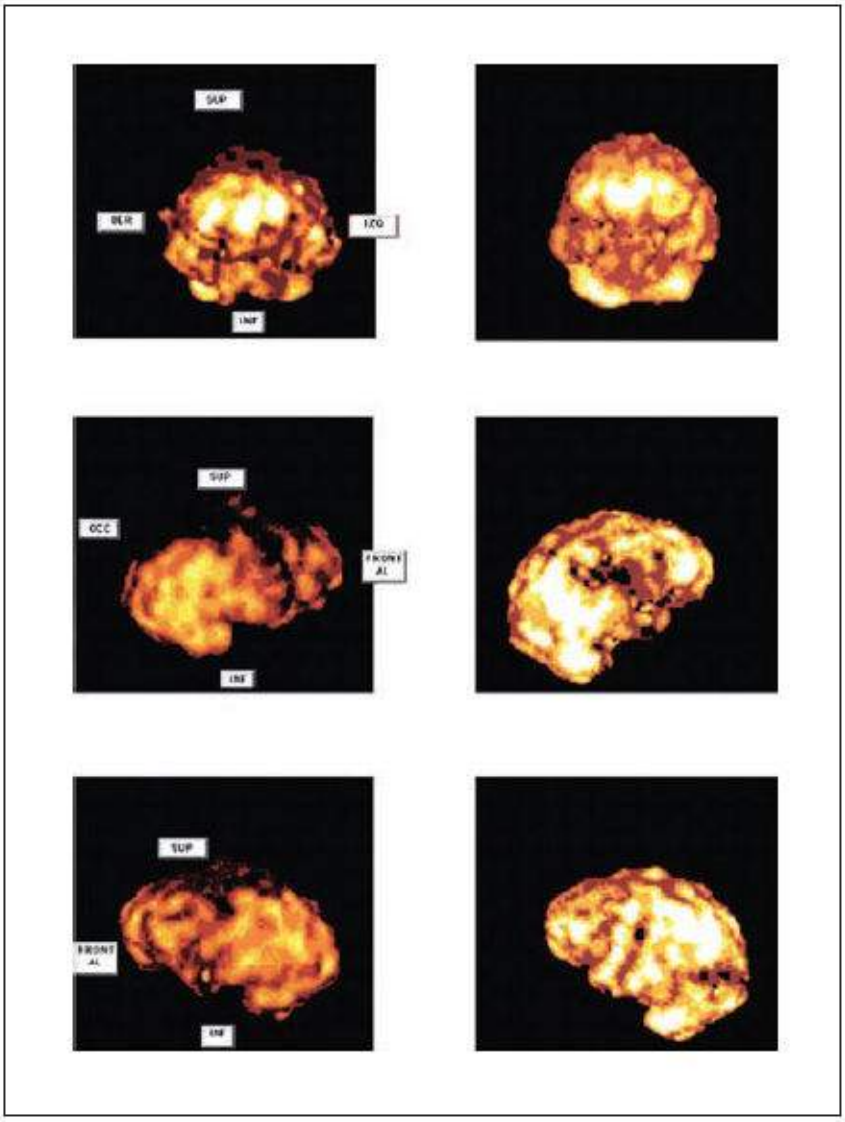

Figure 5.7. SPECT scan of the brain of a student with ADHD before and after supplementing with NADH.

Using SPECT (Single Positron Emission Computed Tomography), a reduced blood flow had been demonstrated in students with ADHD. Figure 5.7 on page 74 shows a SPECT scan of a 22-year-old student with ADHD. The photos on the left side of the chart show a reduced blood flow (dark areas) in the brain. This shortage of blood and oxygen can be overcome by supplementing with NADH, as the photos on the right side of the figure demonstrate. This student took NADH (2 lozenge tablets, for a total of 20 mg) for two weeks, then another SPECT scan was performed. The blood flow in all the brain areas appear normal after application of NADH.

Since the development of NADH, many students have taken this dietary supplement. We have received reports about the

positive effects of NADH in terms of improvement of cognitive and physical performance from the students themselves and also from their parents and teachers.

CHAPTER 6

NADH for the Skin

NADH is also available as a skin serum, which contains only a single active ingredient, namely NADH, as nano particles composed of lipids such as lecithin. By this carrier, the NADH is transported into the skin, where it is taken up by the dermis cells. There, it produces ATP energy and water, which is all the skin needs to stay vital. NADH is able to repair altered skin cells damaged by sunburn, allergic reactions, or exposure to toxins.[1]

WRINKLES

NADH skin serum is effective against wrinkles. After only two weeks of a daily application of a few drops of NADH, the deepness of the wrinkles were diminished, and some disappeared totally.[2]

At the University of Freiburg, in Germany, a study was conducted to prove the efficacy of the NADH skin serum on telangiectasias, common alterations of the skin that are also known as cuperoses or “spider veins.” Thirty-six women with extensive telangiectasias participated in this study. They applied the NADH skin serum daily for six weeks to the area afflicted by spider veins. Before and at the end of the treatment period, pictures of the particular skin area were taken by standardized computerized photography (see Figure 6.1 on page 78). These pictures were then examined in terms of changes of the skin by two independent dermatologists. These examiners judged the NADH skin serum to be very effective, leading to a significant reduction of the spider veins. With some women, they disappeared totally.[3]

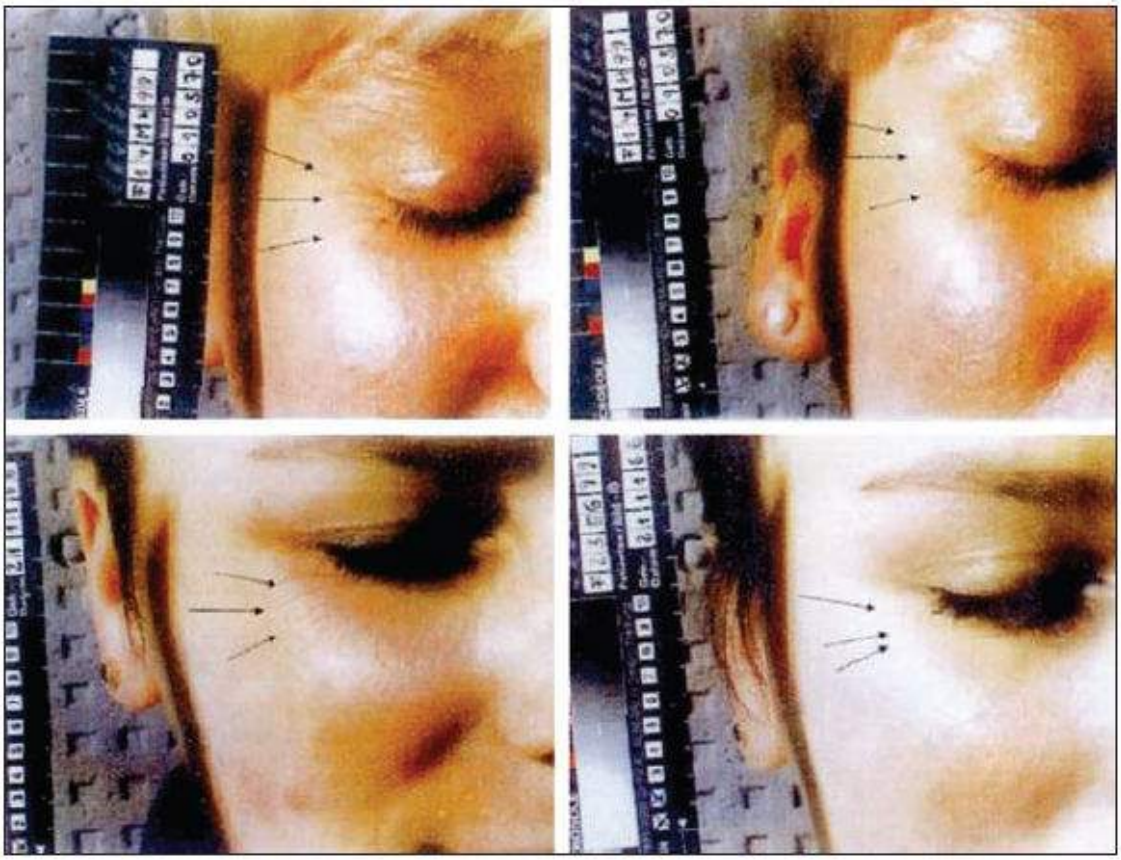

Figure 6.1. Effects of NADH on wrinkles.

ROSACEA

NADH skin serum is effective for rosacea, a severe form of acne. After two weeks of treatment with NADH skin serum, rosacea on the subject's face showed significant improvement. In cases of toxic dermatitis, a significant reduction of the size and severity of the affected skin is possible with NADH.

DIABETIC ULCERS

A further effect of the NADH skin serum was observed with a diabetic patient. The patient was an 80-year-old woman who had suffered from diabetes for many years. She developed open wounds (diabetic ulcers) on her legs about nine months previously. The patient had to cover these ulcers with a sterile bandages, changed several times a day, in order to protect this area from bacterial infections. Infections of diabetic ulcers can become extremely critical as they can cause gangrene formation and necrosis. All therapeutic approaches tried previously did not lead to a wound-healing effect. The patient applied the NADH skin serum to the ulcers two times per day. Two weeks later, the wounds were closed and thus protected from potential infections (see Figure 6.2 below). The healing process continued and was completed after six weeks.

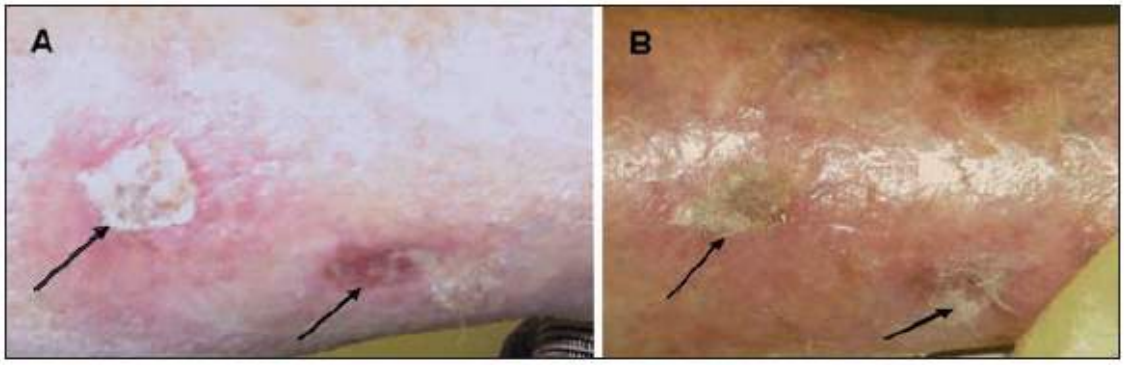

Figure 6.2. Effects of NADH on diabetic ulcers.

SKIN LESIONS

Since the development of the NADH skin serum, we have observed beneficial effects in a variety of other skin lesions, including aging spots, acne, contact dermatitis, and vitiligo (see Figure 6.3 below). A number of women have reported feeling more active and vital about an hour after application of the NADH. They felt like they were getting an energy boost from this cosmetic product.

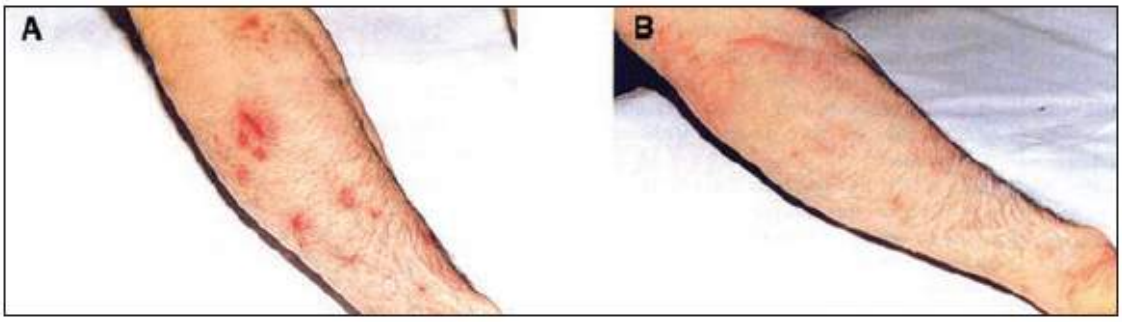

Figure 6.3. Effects of NADH on skin lesions.

This observation was indirect evidence that NADH skin serum was able to penetrate the skin and increase the energy level not only in the dermis but in the entire body.

Application of the skin serum may be a convenient form of getting NADH into the body, particularly for those who dislike swallowing tablets. Because of this activating and energizing effect, it may keep one awake longer in the evening. If this is unwanted, the skin serum should be applied earlier in the day.

CHAPTER 7

NADH to Boost Sex Drive and Increase Longevity

BOOSTING SEX DRIVE

The center for sexual stimulation does not reside in the genital region but in the brain, more precisely, in the hypothalamus. This pea-sized organ is located in the basal part of the brain. The hypothalamus regulates blood pressure, body temperature, and the production of sex hormones. Sexual as well as non-sexual stimulation is generally triggered by the neurotransmitter dopamine. If dopamine is lacking in the hypothalamus, a depressive mood arises, the exact opposite of a exciting and pleasant one. In patients suffering from depression, and particularly in patients with Parkinson's disease, a dopamine deficit has been detected in certain areas of the brain.[1] If the patients obtain L-DOPA (a precursor of dopamine synthesis) as therapy, the dopamine level in the brain increases. Not only are they less depressed, it has been observed with numerous Parkinsonian patients that their sexual activity increased after long-term treatment with higher dosages of L-DOPA.[2]

NADH also stimulates the biosynthesis of dopamine and adrenaline in the brain. Furthermore, NADH enhances the production of nitric oxide (NO), a neurotransmitter that relaxes and dilates blood vessels. As a consequence, the organs get more blood. NADH functions as coenzyme in the biosynthesis of H4-biopterine, a compound necessary for the effectiveness of nitric oxide synthetase, the enzyme which produces NO from oxygen and L-arginine (an amino acid). NADH stimulates the biosynthesis of NO to a much greater extent than any other substance.[3]

By the way, Viagra® (sildenafil citrate) works by a different principle: the active ingredient in Viagra inhibits the enzyme

5,3-phosphodiesterase, which regulates indirectly the degradation of NO. By blocking the catabolism of NO, one may achieve an increase in NO level. However, if the production of NO in the cells is low, for whatever reason, a blockade of its degradation may lead, if at all, only to a small increase. Physiologically, it seems more reasonable to simply enhance the biosynthesis of NO. This can be achieved by supplying the body with NADH and arginine. Arginine is present in almost all proteins, with a very high content found in hazelnuts, peanuts, and almonds. Also, soybeans and lentils contain arginine in higher concentrations.

The release of NO from arginine is stimulated strongly by NADH. More NO in the body causes a higher blood flow through all organs, which means more oxygen is circulated through the body. The more oxygen and NADH the organs have available, the better they are protected because they have a higher ATP energy level.

Numerous consumers of a dietary supplement containing arginine and NADH have reported increases in stimulation, libido, sex drive, and sexual performance. NADH in combination with arginine represents a stimulant for men and women. This combination offers an advantage over prescription stimulants in that it has no side effects or interactions with other drugs.

ORGAN PROTECTION

More than 70 percent of people in the United States take some form of medicine on a regular basis. However, prescription drugs are also the fourth most frequent cause of death. Not a single substance by itself but rather the interactions of multiple drugs taken in conjunction are responsible for many fatalities. Patients as well as health authorities are well aware of the fact that drugs exhibit not only beneficial effects but also adverse reactions.

There is no doubt that pharmaceuticals put a heavy load on the body, particularly if they are taken regularly over many years. The liver and kidneys are the organs exposed to the strongest burden. The liver attempts to detoxify harmful substances and the kidney must excrete them. These organs do not always function in the way they should. For example, certain painkillers cannot be eliminated by the kidneys, so they are deposited in the organ and may eventually damage it. The first filter for neutralizing toxins is the liver. By its various enzymes, the liver tries to transform the many compounds taken as drugs to less harmful ones. However, long-term exposure to drugs strains the capacity of the liver and, as a consequence, the cells and tissues are damaged and eventually destroyed.

In particular, alcohol causes a deterioration of the metabolism and tissue injury in a relatively short time, as its degradation needs a lot of oxygen.[4] Alcohol consumption leads to an oxygen deficiency not only in the liver but also in other organs, particularly in the brain. Consuming alcohol regularly is harmful as alcohol reduces the formation of substances essential for production of ATP energy. A lack of ATP decreases the capacity of the cells to fulfill their important functions.[5] If the ATP level in the cell drops below a certain threshold, the cell dies and liver tissue perishes.[6] This leads to restricted function and finally to a complete failure of the liver. For full functionality, the liver needs sufficient oxygen and ATP energy.

Studies discussed earlier demonstrated that NADH increases ATP levels in heart cells and red blood cells, so it likely it does the same in the liver. And from studies with athletes, we learned that NADH acts like a vacuum cleaner in sucking oxygen into the cells faster—the more NADH a cell has available, the more oxygen it can take up. This phenomenon allows the liver to overcome the increased oxygen demand induced by alcohol. Based on these functions, NADH can protect the liver from damage by alcohol. If liver cells have more NADH available, they produce more ATP and the enzymes for detoxification function better. NADH also reduces the time of exposure to harmful substances (such as alcohol) by degrading them more quickly.

A combination supplement containing NADH and chlorophyll (the photosynthesis chemical in plants) has been developed for use in detoxification. Chlorophyll, based on its physical and chemical features, can penetrate fat tissue. In most cases, toxins (particularly organic ones, such as many drugs as well as alcohol) are deposited there. Chlorophyll can enter these cells and bind these harmful compounds, neutralize them, and eliminate them from the fat tissue. Due to these features, chlorophyll protects lipid tissue. The combination of NADH and chlorophyll is a dietary supplement for protection of the brain, liver, and kidney.

ANTI-AGING BENEFITS

The term *anti-aging* has been created to fulfill a desire of our society: people want to live longer without getting older and the quality of life should, of course, be more than excellent. Many people don't want to give up anything even at a very old age. Numerous ideas are praised as concepts for anti-aging and foisted on the public, including multivitamins and other supplements, hormone replacement therapy (HRT), and even toxins such as Botox (botulinum toxin), a poisonous substance that relaxes muscles and is commonly used to stop wrinkle formation. Unfortunately, most of the products presently marketed as anti-aging substances and/or procedures are lacking the scientific proof of their efficacy.

Is the idea of anti-aging pure wishful thinking? To answer this question, we have to look at the factors that influence life expectancy. The life span of humans is dependent on three factors: genes, lifestyle, and medical treatment of ailments. Experts believe that genetic factors contribute 40 to 50 percent to one's life span, and lifestyle about 30 to 40 percent; medical treatments amount to only 10 percent, yet most of the costs for life extension are spent on the medical treatments. It would be much more reasonable to invest in lifestyle, the social environment, and the world around us. By this approach, life-threatening risk factors could be reduced and enormous amounts in health-care costs would be saved. For example, excess weight, smoking, alcohol, drugs, and a sedentary lifestyle shorten one's life span. Weight reduction, refraining from smoking and alcohol, and physical activities on a daily basis increase the probability of a longer and healthier life.

But from all the ideas about health-supporting factors, not a single one has been proven scientifically to extend the life span. To do this, one has to document that cells, tissues, organs, and the entire organism live longer under a particular regimen. Do substances exist that can keep cells alive for a longer period of time? The answer is: Yes, there are—

namely, the molecules in the cell that store energy. The most important of these is ATP (adenosine triphosphate); the more ATP a cell has available, the better it can perform its functions and the longer it can live. If the ATP level falls below a certain threshold, the cell dies.

We can increase the ATP level in a cell by supplementing with NADH. NADH, the biological form of hydrogen, reacts with oxygen present in all cells to form ATP. ATP concentration in cells can be increased by giving them NADH.[7] Studies using isolated heart cells showed an increase in ATP in the cells when exposed to NADH. As a likely consequence of the increased ATP level, the heart cells exhibited a stronger viability and a longer life span after incubation with NADH. This life-extending effect of NADH could be demonstrated with other cell types as well.

Preliminary findings from a University of Graz study indicate that transplantable organs, such as hearts, can be preserved for a longer period of time by adding NADH to the preserving solution. According to these experiments, the functional capability and vitality of the heart can be kept longer as the heart gains more energy by NADH. What has been shown for the heart, the most important organ of our body, should work also for other organs.

Conclusion

NADH is the only scientifically proven substance on earth that increases ATP energy in a cell. Having more energy, the cells function better and so will the tissues and organs and, in fact, the whole body. NADH provides you with more energy, whether you are a highly conditioned athlete or a chronic fatigue syndrome sufferer. All people can benefit from NADH, particularly those with an energy-draining lifestyle. For elderly people, many of whom suffer from depression, Parkinson's disease, or Alzheimer's dementia, NADH may be extremely beneficial in giving them a greater vitality and a much better quality of life.

NADH is important for people today to preserve and optimize their health. And NADH, based on its multiple beneficial effects, should gain an even greater importance for people in the future. The energy-increasing effect of NADH as well as its capability to repair damaged cells will have an enormous impact for preventing diseases, particularly for chronic diseases such as heart disease, cancer, arteriosclerosis, and rheumatoid arthritis. Prevention of disease is definitely the best and most cost-saving form of medicine.

All people with a genetic predisposition and an unhealthy lifestyle should receive NADH as a preventive supplement to reduce the elevate risk of developing one of these diseases. By this approach, the incidence of heart attacks or cancer may be reduced considerably and could save enormous health-care costs. The long-term use of a natural, safe, and effective energizing substance such as NADH could prove to be a quantum leap in medicine.

NADH—the biological hydrogen—generates energy for every living cell. With NADH as fuel for cellular energy production, the secret of our life energy has been revealed. I hope you will take this secret as a personal message to stay vital and healthy and maintain a high quality of life for as long as possible.

Glossary

Akinesia. Loss of normal motor function, resulting in impaired muscle movement; a term used in neurology to denote the absence (or poverty) of movement.

Amino acids. Building blocks of proteins, they also act as intermediates in metabolism.

Antioxidants. Substances that prevent oxidation. For example, if fats or butter are oxidized, they become rancid. Nutrients in our foods that can prevent or slow oxidative damage to our body are called antioxidants.

Apoptosis. A form of programmed cell death in multicellular organisms. It involves a series of biochemical events that lead to a variety of morphological changes (including blebbing), changes to the cell membrane (such as loss of membrane asymmetry), and finally to the death of the cell.

Arginine. A nonessential amino acid, meaning it can be manufactured by the human body and does not need to be obtained directly through the diet. Animal sources of arginine include dairy products, meats, poultry, wild game, seafood, wheat germ, buckwheat, oatmeal, nuts and seeds, and soybeans.

ATP. The abbreviation for adenosine triphosphate. ATP is the energy for life, because it is present in every living cell and catalyzes all physiological reactions that need energy. Every physical and mental performance (e.g., muscle contraction or thinking) needs energy that can only be supplied by ATP.

Carcinogen. Refers to any chemical and physical substance (e.g., tobacco smoke, asbestos, or radiation) that is

an agent directly involved in the promotion of cancer or in the facilitation of its propagation. This may be due to the ability to damage the genome or to the disruption of cellular metabolic processes.

Cellular immune system. Also called cell-mediated immunity, it is an immune response that does not involve antibodies but rather involves the activation of certain white blood cells, such as T-lymphocytes and macrophages. Cell-mediated immunity is directed primarily at microbes that survive in macrophages and phagocytes, and microbes that infect nonphagocytic cells. It is most effective in removing virus-infected cells, but also participates in defending against fungi, protozoans, cancers, and intracellular bacteria.

CFS. The abbreviation for chronic fatigue syndrome, a condition characterized by extreme exhaustion and the inability to work. In Europe, CFS is better known as myalgic encephalomyelitis (ME). Worldwide, a couple of hundred million people suffer from CFS.

Coenzyme. A necessary component for an enzyme to become active. You can compare enzymes and coenzymes with the engine in a car. The enzyme is the engine and the coenzyme is the spark that triggers the explosion of the fuel. Coenzyme molecules are often vitamins or are made from vitamins. Many coenzymes contain the nucleotide adenosine as part of their structures, such as ATP, coenzyme A, and NAD+.

Cytokine. A category of signaling molecules in our body, which, like hormones and neurotransmitters, are used extensively in cellular communication. While hormones are secreted from specific organs to the blood, and neurotransmitters are related to neural activity, the cytokines are a more diverse class of compounds in terms of origin and purpose. They are produced by a wide variety of cell types, in particular, by white blood cells. Cytokines are critical to the development and functioning of both the innate and adaptive immune response.

Cytotoxic. Toxic to cells, cell-killing. Any agent or process that kills cells can be called cytotoxic. Chemotherapy and radiation are forms of cytotoxic therapy.

DNA. Deoxyribonucleic acid is a nucleic acid that contains the genetic instructions used in the development and functioning of all known living organisms and some viruses. The main role of DNA is the long-term storage of genetic information, the instructions needed to construct other components of cells, such as proteins. The DNA segments that carry this genetic information are called genes.

Dopamine. A hormone and neurotransmitter occurring in a wide variety of animals, including both vertebrates and invertebrates. Dopamine is produced in several areas of the brain. As a chemical messenger, dopamine is similar to adrenaline and affects brain processes that control movement, emotional response, and the ability to experience pleasure and pain.

Enzymes. Substances that catalyze metabolic processes in the body. Without them, our daily food cannot be digested and no vitamins or minerals essential for life can be used. Usually, enzymes are large molecules such as proteins to which the substance to be metabolized is bound and turned over into another substance.

Free radicals. Highly reactive molecules that can interfere with almost all components of body cells. They can be formed when oxygen interacts with certain molecules. Once formed, free radicals can start a chain reaction, like dominoes. Their chief danger comes from the damage they can do when they react with important cellular components such as DNA or with the cell membrane. Cells may function poorly or die if this occurs. To prevent free radical damage, the body has a defense system of antioxidants.

Glucose. Also known as grape sugar, it is an important carbohydrate in biology. The living cell uses glucose as a source of energy and as a metabolic intermediate.

Humoral immune system. The aspect of immunity that is mediated by antibodies (as opposed to cell-mediated immunity, which involves T-lymphocytes) produced in B-lymphocytes, a subgroup of white blood cells. They secrete antibodies that bind to the surfaces of invading microbes (such as viruses or bacteria), which flags them for destruction.

Intravenous (IV). The giving of liquid substances directly into a vein.

Isoflavones. A class of rather small, usually yellow-colored organic compounds related to the flavonoids. Isoflavones and isoflavone-rich foods possess activity against cancer.

Krebs cycle. A metabolic roundabout cycle that is the final common catabolic pathway for the oxidation of fuel molecules taken up by nutrition. In the course of the cycle, four oxidation-reduction reactions take place to yield reduction potential in the form of three molecules of NADH and one molecule of FADH2. The Krebs cycle is also called the citric acid cycle or tricarboxylic acid (TCA) cycle but is most well-known under the name of its discoverer, Sir Hans Krebs.

Lipids. Organic molecules of fat occurring in the body. They are hydrophobic, meaning that they don't like water. This group of molecules includes fats and oils, waxes, phospholipids, steroids (like cholesterol), and some other related compounds.

Metastasis. The process by which cancer spreads from the place at which it first arose as a primary tumor to distant locations in the body. Metastasis depends on the cancer cells acquiring two separate abilities, increased motility and invasiveness. Cells that metastasize are basically of the same kind as those in the original tumor. If a cancer arises in the lung and metastasizes to the liver, the cancer cells in the liver are lung cancer cells.

NADH. The abbreviation for nicotinamide adenine dinucleotite hydride, also known as coenzyme-1. Nicotinamide

is another term for vitamin B_3, hence NADH can be regarded as coenzyme form of B_3.

Neoplastic. From the Greek meaning “new growth.” The abnormal proliferation of cells, resulting in a structure known as a neoplasm. A precise and all-encompassing definition of neoplasm has proven elusive, but the definition of the British oncologist R.A. Willis is widely cited: “A neoplasm is an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissues, and persists in the same excessive manner after cessation of the stimulus which evoked the change.“

Neurotransmitters. Chemicals that are used to relay, amplify, and modulate signals between a neuron and another cell.

Nicotinamide. Also known as niacinamide, this is the amide of nicotinic acid (vitamin B_3), a water-soluble vitamin and part of the vitamin B complex. In cells, niacin is incorporated into nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP). NAD+ and NADP+ are coenzymes in a wide variety of enzymatic oxidation-reduction (redox) reactions.

Oxidation. The interaction between oxygen molecules and all the different substances they may contact, from metals to living tissue. In a living organism, oxidation (particularly oxidation of lipids of the cell membrane) can lead to severe damage and even cell death.

Oxidative phosphorylation. A metabolic pathway that uses energy released by the oxidation of nutrients to produce adenosine triphosphate (ATP), the molecule that supplies energy. Although the many forms of life on earth use a range of different nutrients, almost all carry out oxidative phosphorylation to produce ATP.

Phagocyte. A biological cell that ingests and destroys foreign matter, such as microorganisms and debris, by a process called phagocytosis (from the Greek meaning “cell eater”).

Reduction. Removing oxygen from a compound. For example, if you remove oxygen from water, you get pure hydrogen, which is the strongest reducing agent. The biological form of hydrogen is nicotinamide adenine dinucleotide hydride (NADH), which is the most potent biological reducing agent (equivalent to the strongest antioxidant).

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About the Author

George D. Birkmayer, M.D., Ph.D., is a professor at the University of Graz, in Austria,. He is also visiting professor at the University of Beijing, Xi'An, and Canton, in China, and president of the International Academy of Tumor Marker Oncology in New York.

Dr. Birkmayer discovered the therapeutic effect of NADH (Coenzyme-1) and developed the stabilized and orally absorbable form of NADH for therapeutic application. He is the author of more than 150 major research papers and more than 100 scientific articles in the areas of cancer diagnosis and neurochemistry and neuropharmacology related to Parkinson's disease and Alzheimer's disease.