"At the cellular level, energy is used to make new proteins, to bring nutrients into a cell and expel cellular wastes, to repair damaged DNA, to synthesize neurotran smitters, etc

The energy source for all these levels is the same - it is the bio-energy molecule ATP (adenosine triphosphate) the "universal energy currency of the cell"567.

3.2 MAJOR PATHWAYS OF ENERGY METABOLISM

Glucose is oxidised by all tissues to synthesise ATP. The first pathway which begins the complete oxidation of glucose is called glycolysis. The normal pathways are briefly described320, 545:

3.2.1 Glycolysis

Glycolysis (the breakdown of glucose to pyruvate and lactate, occurs in the cell cytoplasm): Glucose + 2 ATP + 4 ADP + 2 NAD -> 2 Pyruvate + 2 ADP + 4 ATP + 2 NADH + energy. Oxidation of glucose is known as glycolysis. Glucose is oxidized to either lactate or pyruvate. Under aerobic conditions, the dominant product in most tissues is pyruvate and the pathway is known as aerobic glycolysis. When oxygen is depleted, as for instance during prolonged vigorous exercise, the dominant glycolytic product in many tissues is lactate and the process is known as anaerobic glycolysis. "These studies demonstrate that orderly glycolysis in the erythrocyte is regulated by the NAD-to-NADH ratio and also provide a method that makes possible the in vitro study of erythrocyte glycolysis."235

The conversion of pyruvate to lactate, under anaerobic conditions, provides the cell with a mechanism for the oxidation of NADH (produced during the G3PDH reaction) to NAD which occurs during the LDH catalyzed reaction. This reduction is required since NAD is a necessary substrate for G3PDH, without which glycolysis will cease. Normally, during aerobic glycolysis the electrons of cytoplasmic NADH are transferred to mitochondrial carriers of the oxidative phosphorylation pathway generating a continuous pool of cytoplasmic NAD.546, 733

3.2.2 Gluconeogenesis

Gluconeogenesis is the biosynthesis of new glucose, (i.e. not glucose from glycogen). The production of glucose from other metabolites is necessary for use as a fuel source by the brain, testes, erythrocytes and kidney medulla since glucose is the sole energy source for these organs. Under fasting conditions, gluconeogenesis supplies almost all of the body's glucose to the brain as energy from ketone bodies which are converted to acetyl-CoA. Synthesis of glucose from three and four carbon precursors is essentially a reversal of glycolysis. The three

reactions of glycolysis that proceed with a large negative free energy change are bypassed during gluconeogenesis by using different enzymes. Lactate is a predominate source of carbon atoms for glucose synthesis by gluconeogenesis.730, [733]

3.2.3 The Pyruvate Dehydrogenase Complex

The pyruvate dehydrogenase complex (which oxidizes pyruvate to enter the citric acid cycle, operates only under aerobic conditions): Pyruvate + NAD + Coenzyme A -> CO2 + acetyl-CoA + NADH + energy. Cofactors required for pyruvate dehydrogenase include five different coenzymes namely: thiamine pyrophosphate (TPP) from thiamin; flavine

adenine dinucleotide (FAD) from riboflavin; Coenzyme-A (CoA), from pantothenate; nicotinamide adenine dinucleotide (NAD), from vitamin niacin and alpha-lipoic acid.544

3.2.4 The Citric Acid Cycle (Krebs Cycle)

The citric acid cycle (which completes the oxidation of carbohydrates and other substrates to carbon dioxide, occurs in mitochondria of cells): Acetyl-CoA + 3 NAD + FAD + ADP -> 2 CO2 + Coenzyme A + 3 NADH + FADH2 + ATP. Regulation of the TCA cycle, like that of glycolysis, occurs at both the level of entry of substrates into the cycle as well as at the key reactions of the cycle. Fuel enters the TCA cycle primarily as acetyl-CoA. The generation of acetyl-CoA from carbohydrates is, therefore, a major control point of the cycle. This is the reaction catalyzed by the PDH complex. The PDH complex is inhibited by acetyl-CoA and NADH and activated by non-acetylated CoA (CoASH) and NAD. Since three reactions of the TCA cycle as well as PDH utilize NAD as cofactor it is not difficult to understand why the cellular ratio of NAD/NADH has a major impact on the flux of carbon through the TCA cycle.737

3.2.5 Electron Transport and Oxidative Phosphorylation

Mitochondrial oxidative phosphorylation in vivo is dependent on the degree of reduction of the intramitochondrial reducing power ([NADH]/[NAD], cytoplasmic energy state ([ATP]/[ADP][Pi]) and intracellular oxygen pressure. Electron transport and oxidative phosphorylation (occurs in membranes of mitochondria in cells only under aerobic conditions). Nutritional implications and chemical structures are NAD and FAD. While the large quantity of NADH resulting from TCA cycle activity can be used for reductive biosynthesis, the reducing potential of mitochondrial NADH is most often used to supply the energy for ATP synthesis via oxidative phosphorylation. Oxidation of NADH with phosphorylation of ADP to form ATP are processes supported by the mitochondrial electron transport assembly and ATP synthase, which are integral protein complexes of the inner

mitochondrial membrane. Oxidative phosphorylation traps this energy as the high-energy phosphate of ATP. In order for oxidative phosphorylation to proceed, two principal conditions must be met. First, the inner mitochondrial membrane must be physically intact so that protons can only re-enter the mitochondrion by a process coupled to ATP synthesis. Second, a high concentration of protons must be developed on the outside of the inner membrane.731, [742] "A prolonged decrease in ATP levels underlies a number of neurodegenerative disorders. Defects in oxidative phosphorylation are associated with a number of neurodegenerative disorders."748

"The precise relationship between mitochondrial DNA mutations, impairment of oxidative phosphorylation and clinical phenotypes is not well understood. The prevailing view is that defects in ATP generating capacity due to mitochondrial DNA defect leads to energy failure, cellular dysfunction and eventually cell death in the affected tissues."765

Pyridine nucleotides (NAD etc) are mostly stored within mitochondria where they are involved in different functions ranging from energy metabolism to cellular signalling. Here we discuss the mechanisms of mitochondrial NAD(+) metabolism and release that may contribute to the crucial roles played by these organelles as triggers or amplifiers of physiological and pathological events".687

The mitochondria are small structures which are present in all cells. The quantity of mitochondria varies amongst the different types of cells. Liver cells, for example, contain many more mitochondria than sperm cells129. The energy that is generated, is apportioned for use in cellular activity, for storage as chemical compounds that are rich in energy (like ATP and NAD derivatives), and the remainder is released as heat39. The primary "objective" of the energy metabolism is the manufacturing of ATP (about 50kg per day in the average human being) thereby providing the power for all cellular activities370.

Ninety per cent of the body's energy is provided by the mitochondria's process of oxidative phosphorilisation. It is an extremely effective system for providing sufficient energy, to maintain the body's structure and functioning, and for regulating the body's temperature. The process consists of two metabolic processes that are closely linked to each other, i.e. the citric-acid cycle and the electron-transfer chain. In complex I of the electron-transfer chain, NAD to NADH is involved; in the citric-acid cycle three NAD to NADH compounds are involved82. The citric-acid cycle cannot function without the availability of NAD and NADP. Slight deviations in the activity of the mitochondria can lead to weakness, fatigue and cognitive problems51, [68].

Mitochondria have a crucial role both in energy production and the viability of the cell and recently mitochondria have been implicated in programmed cell death

(apoptosis).

Research indicates that 10% of the world's population is suffering from NED, mostly manifesting as chronic fatigue syndrome (CFS), substance abuse, depression, stress, anxiety and various other chronic illnesses. NED is a spectrum disorder, which is initially difficult to understand. Grandmother might, for example, be suffering from NED masked as obesity, her son's workaholism masked his NED and her granddaughter might be a drug addict. The daughter-in-law is a religious addict, who never misses any prayer meeting. All of them wonder where the granddaughter could pick up this dirty and sinful habit. All four of these seemingly unrelated conditions are masks of NED, which are only revealed on different levels and in different ways. This e-book will clearly demonstrate the golden thread of NED that exists amongst these various "unrelated disorders" and the effective role of NAD Therapy in the treatment thereof.

NAD Energy Deficiency (NED) differs from energy deficiency that is defined as the lack of food and in its worst state is called famine. **NED is the cellular energy metabolic state, irrespective of the amount of food available or consumed, that develops and persists when there is not enough molecules of NAD and the other energy metabolic cofactors or energy factories (mitochondria) to convert the organic energy in food to chemical energy for use in the cells, tissues and organs.**

Restricting NAD recycling can lead to symptoms like problems with memory, irritability, problems with concentration, depression, apathy, low intellectual energy, increased anxiety and panic, increased craving for alcohol, sugar and nicotine, decreased sex drive and increased premenstrual tension214.

· "In the case of hypoxia, or other causes of inhibition of the electron transport chain, NADH accumulates and the supply of NAD is depleted. This pushes the balance between pyruvate and lactate dramatically in favour of lactate further exacerbating its production in these circumstances. This change also occurs with alcohol abuse with alcohol dehydrogenase depleting NAD and producing NADH.642"

- **5.2 BIOCHEMICAL FUNCTIONS OF NAD**
- NAD was the first co-enzyme to be identified in 1905 by Harden and Young138. NAD has more than 100 functions in the human metabolism. Even the activity of the citric-acid cycle, which is found in most cells, becomes restricted in the lack of NAD and NADP154. The body constantly requires NAD and if the NAD level becomes too low, the need for it
- is activated in the primitive part of the brain. This biochemical action cannot be controlled by the mind or changed by willpower. Alcohol and the metabolites, which it creates, suppress this need for NAD. Excessive

exercising and the associated secretion of endorphins also suppress the need for NAD51.

- **5.2.1 Metabolic Detoxification of Chemical Substances**
- NAD has already been used successfully since 1939, for the short-term treatment of alcoholism51. O'Halleren was however the acknowledged leader in treating various types of substance dependencies with the aid of NAD supplements. He used NAD to treat alcohol-, heroin-, cocaine-, morphine-, meperidine-, codeine-, amphetamine-, barbiturate- and sedative dependents166. NAD does not have the same side-effects as nicotinic acid at high dosages, like serious flushing and the release of histamine211.
- The intracellular metabolism of alcohol, and possibly also of other chemical substances, requires NAD or derivatives thereof, in order to take place. Ninety per cent of alcohol is absorbed almost immediately in the body's cells; the remaining 10% is discharged mainly in the urine. Acetaldehyde is the first metabolite of various chemical substances, including alcohol, that is produced26, 133, 166, 173, 176, 227, 249. Acetaldehyde is also formed during stress. Acetaldehyde is used as a preservative in certain dairy products214. The last step in the metabolic detoxification process occurs in the citric-acid cycle, where three NADs are involved in the process. This cycle is also responsible for the conversion of proteins, carbohydrates and fats into ATP. This is a purely biochemical autonomic reaction, and neither the person's will or any other form of control can be exercised over it. The biochemical reactions can be simplified as follows:
- **Chemical Substance + NAD -> Acetaldehyde + NAD -> Acetate + CoA -> Acetyl- CoA +3NAD(H) -> ATP + H2O + CO2 + Heat**
- Ethanol toxicity is closely related to its metabolism in the liver. The elevated NADH/NAD ratio (i.e. NAD deficiency) results in alterations of the intermediary metabolism of lipids, carbohydrates, proteins, purines, hormones and porphyrins. This shift in metabolic pathways results in hyperlactacidaemia, lactacidosis, ketosis and hyperuricaemia. Furthermore, excess NADH can results in free radical production491, 492, 493.
- The NADH that builds up, e.g. during e.g. alcohol metabolism, will drive pyruvate to lactate which can lead to acidosis. The pyruvate is now not available for gluconeogenesis and if, as is common in serious alcoholism, the patient is not eating properly, hypoglycemia can result. The high NADH/NAD ratio will affect other processes such as b-oxidation. One clinical manifestation is liver disorders associated with alcoholism: fatty liver, alcoholic hepatitis and, sometimes, cirrhosis. The burden on oxidizing systems also leads to increased use of the P450 or microsomal oxidizing system which can have important effects on steroid metabolism

and other processes involving this system[491, 492, 493].

- NAD and NADP, which are pyridine nucleotides, are rated as being amongst the important high energy compounds in the biochemistry of organisms[138]. The reduction of NAD plays an important part in the citric-acid cycle and contributes to the production of 22 molecules of ATP from one molecule of glucose[38]. NAD and its derivatives NADH, NADP and NADPH have regulatory functions in the generation of triose phosphates and pyruvate from glucose[607]. NAD is reduced to NADH in the metabolism of glucose. The hydrogen molecule is obtained from the metabolism of fats, carbohydrates and proteins. The activated NADH plays a part in several critical bodily functions, amongst others, in the continued production of ATP, which is the basic energy compound in the body[45]. NAD plays an important role in the release of energy from carbohydrates, fats and proteins[137]. In the absence of oxygen, pyruvate must be converted to lactate to regenerate NAD from NADH in the cytoplasm. In the presence of oxygen, the mitochondria can reoxidize cytosolic NADH by an indirect process, involving the mitochondrial "shuttle systems"[348].
- **5.2.5 Improving Brain Functions**
- The brain is metabolically speaking one of the most active organs in the body and consumes approximately 20% of all energy generated[21, 350]. Its weight-to-energy ratio is ten times more than that of most other organs. The brain does not really have any reserves of energy, in the true sense of the word, and must therefore be supplied continuously with energy by the body. The brain, as a whole, consumes approximately 4 x 1021 molecules of ATP per minute and this increases during REM sleeping. During the first ten years of a child's life, the brain consumes up to twice as much energy as during adulthood[212]. When pyruvate oxidation is impaired, glycolysis will run faster than normal to try to make up for deficient ATP production. This will cause more production of lactate. The brain relies on oxidation of glucose as an energy source and has a limited ability to oxidize fatty acids. In cases of severe energy depletion mental retardation is not surprising[348]. NAD plays an important part in the production of ATP in cells[38].
- Derivatives of niacin, mainly in the form of NAD and NADP coenzymes, are found abundantly in brain tissue. In the case of niacin deficiency, the brain's supply of NAD declines sharply and the functioning of the brain is disturbed; malfunctioning of the brain (dementia) is indeed one of the primary characteristics of pellagra. If the NAD deficiency lasts for an extended period, permanent brain damage develops[144].
- Scientists have discussed the possible use of NAD for the treatment of neurodegeneration[155] and the improvement of brain functions. NADH plays a role in the synthesis of the neurotransmitters, i.e. noradrenaline and dopamine, which are important for maintaining a positive state of

mind42. South African research on NAD, that was conducted for the manufacturer, also confirms the normalising effect of NAD on the neurotransmitters, i.e. dopamine, adrenaline and noradrenaline. NAD probably plays a role in the production of serotonin and other neurotransmitters in the brain214.

- **5.6.1 Patents for NAD Therapy** NAD was patented in 1964, for the treatment of drug dependency. It was registered in 1966, for the treatment of alcoholism. The patent for the use of NAD supplementation in the treatment of ileus and shock was awarded in 1967. The patent for use in the treatment of schizophrenia was also approved during the same year. Shortly thereafter, the patent for the use of NAD in the treatment of arthritis was also approved. A patent is registered which generates NAD or nicotinamide adenine dinucleotide phosphate (NADP) in the body344.

- **5.6.4 Safety of NAD Therapy**
- NAD Therapy has been used intravenously in South Africa since 1974 and, according to the manufacturer, no side-effects have yet been reported by clinicians. More than 15 000 NAD supplements (500 mg per drip) have been administered intravenously at Nutrimalaika since 1989, to more than 6 000 patients, who ranged in age from as young as 9 - 90. Furthermore, no race-, gender- or age-related contra-indications were encountered. Since 1995 many patients have used 50mg of NAD orally dissolved in 340ml of carbonated sodawater. This has now become the norm because almost all of the 6 000 patients at Nutrimalaika and those of the 120+ participating private practitioners have changed to the 50mg NutriNAD capsules specifically formulated for such use.

- **5.6.6 Alternative Names for NAD** NAD is also referred to in literature as diphosphopyridine nucleotide (DPN), nadide, adenine-D-ribose-phosphate-phosphate, cozymase, coenzyme 1, D-ribose-nicotinamide, vitamin PP and enzopride.

- **5.6.8 Contra-indication for NAD Therapy**
- According to the manufacturer, no contra-indication has been reported since 1974 by any clinician, for the use of NAD. NAD must however be used with care in persons with Gilbert's disease, in whom it can cause serious abdominal pain65.

5.8 POPULARITY OF NAD THERAPY

Although NAD Therapy were used in the treatment of alcoholism since 1939, patented in 1964 and the NAD vials officially registered in 1974 in South Africa it is still relatively unknown by treatment professionals. A possible explanation is that treatment professionals not working with substance dependency or those

working with substance dependency from the moral treatment approach would probably be not aware of NAD Therapy and its energy related characteristics. NAD has been available as oral supplements in capsule form since 1997 in South Africa. An international researcher ascribes the relative unpopularity of NADH, also applicable to NAD therapy, to its high cost of around 10,000 dollars per kilogram346. Several laboratories around the world are currently involved in studies for the development of NAD analogues for therapeutical applications92. Although NAD is part of all nature and man since creation, NAD Therapy is relatively new. The chronological course of NAD reveals that it only picked up momentum since the ground breaking article of Prof Cleary in 1986.

· 1905 The coenzyme nicotinamide adenine dinucleotide (NAD) is identified

· 1939 NAD is first used for the treatment of alcoholism

· 1955 Dr Hoffer uses NAD for the treatment of schizophrenia

· 1961 Dr O'Halleren uses NAD-drips for the treatment of all chemical addictions

· 1970 The role of the mitochondria in various diseases are outlined

· 1974 The NAD-drips are registered and manufactured in South Africa for the treatment of acute and chronic alcoholism

· 1986 Prof Cleary writes the first article on NAD Deficiency Diseases

· 1989 Alkogen is founded for the outpatient treatment of all chemical addicts with NAD-drips In May 2004 the name is changed to Nutrimalaika.

· 1993 Mitochondrial DNA are identified as mainly maternally inherited

· 1994 Patients with a variety of disorders are treated at Alkogen with NAD-drips

· 1997 Alkogen Products manufactures the capsule MultiNAD and other nutritional supplements containing the metabolic energy cofactors

· 2000 The Afrikaans edition of this NAD Therapy e-book was published

· 2002 The first edition of this NAD Therapy e-book is published in which more than 100 disorders relating to NAD Deficiency are discussed

· 2003 Alkogen Products manufactures the capsule NutriNAD with 50mg pure NAD replacing the NAD-drips in the Alkogen Products treatment program

· 2003 Prof Cleary published the first international article on Alkogen's NAD

Therapy

· 2003 Nutrimalaika, the nurses-led centres, is founded for the treatment of infants and children up to 12 years, old suffering from NED with MalaikaNAD (especially formulated for children) and NutriNAD supplements.

- The Coin of Life: "NAD+ and ATP are the energy currency for the cell. Money is a medium of exchange. People assign work for us to do, we receive money for doing it, and we convert that money into things we want or need. The cell takes its energy source, converts it into NAD(H) and ATP, and then uses them to perform needed tasks in the cell. NAD+ and ATP are not the only carriers of energy, but they are the major ones. (Basic Energy Concepts. ?000 Timothy Paustian, University of Wisconsin-Madison)
- Join the League: The potential of NAD and niacin therapy to treat diseases is now going forward in South Africa. Theo Verwey and his group of clinicians are now the future of this movement to reform medical therapeutics. It is the concept of NAD as a medicine, which must not be ignored: the needed research must be allowed, encouraged, the results evaluated, acknowledge and passed on to the young physicians of today. (Prof JP Cleary MD)
- Buy you Sex Performance: If we take sex as an example, it is experienced by persons with low energy levels as playing on a jungle gym. For persons with high energy levels sex is experienced as a Godly miracle and it makes the couple transcends. (Theo Verwey, MSc)
- Daily Needed: Research indicated, that the average person requires approximately 50 kg of adenosine triphosphate (ATP), which is the basic form of chemical energy for all life, every day to be able to function. Almost 36 kg of NAD is used in the cells, to produce the ATP. In order to accomplish this, the NAD must be recycled in the body. The average person's body contains approximately 16g of NAD and this must be recycled 2 160 times, to enable the body to produce enough energy. (Theo Verwey, MSc)
- Social Investment: It's simple. NAD is a coenzyme facilitating the process where sugar (pyruvate) transforms to lactate. The heart muscle only uses lactic acid as its major source of energy. Two well-known factors reduce NAD in the body and that is alcohol (part of the liver detox process) and exercise. (Dr George Coetzee, MBChB)
- Best Value: To my astonishment and delight there were almost an immediate response and patients who would ordinarily take 3 to 6 months to shows an adequate response to vitamin B3 were responding on NAD in days and weeks... I then went through a most terrible period because my supplies of NAD ran out and I had to deal with my patients who had done so well relapse back into their original disease. My patient we had discharged into the community had to be re-admitted, had to be returned

to the mental hospital where she died several years later. She had not responded to vitamin B3 but had to NAD.(Dr Abram Hoffer MD PhD FRCP)

- Higher Quality of Life: The greater the amount of usable metabolic energy and available quantity thereof, the higher the quality of life and functioning. The brain, for example, uses ten times more metabolic energy than any other organ and has a very limited supply of metabolic energy, which has to be replenished continuously.(Theo Verwey, Clinical Psychologist and NAD Expert (Theo Verwey, MSc)
- Essential Ingredient: "Nicotinamide Adenine Dinucleotide (NAD) is most important for energy. If you have too little NAD, some of your enzymatic reactions do not function and then you cannot produce energy. You cannot produce ATP. NAD supplements must also be added to the minimum maintenance. NAD is a very particular ingredient; it is an essential ingredient of your body. If you do not have it, none of your systems function and this includes your brain. If you do not have any NAD, you die; it is as simple as that." (Dr Henry Davis,MBChB - Behavioural-Genetic Perspective, In D. Steyn & T. Verwey, Dreams for Fragile people.)
- The richest man is the man who invests in himself, his family and his business. Good luck for the man who does not invest wisley with foresight. Albert Einstein said: "Intellectuals solve problems; Geniuses prevents them."
- Desire has successfully transformed the old Alkogen Treatment Network into Nutrimalaika NAD Energy Nutrition Shop - www.nutrimalaika.biz. For the last 7 years at Nutrimalaika she sheared in the joy of children and parents gaining a renewed life with the energy provided by NAD Nutrition.

Síndrome de Abstinencia del Alcohol

Volver al artículo.

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Change = discomfort + vision + first steps

Drugs to get off drugs

CRAVINGS

POST ACUTE WITHDRAWALS

SUCCESS OF TRADITIONAL TREATMENT

CUTTING EDGE OF DETOX

NO CONTRA INDICATIONS NO SIDE EFFECTS

Fears
Safety, different