4

Archaeal Digoxin and Regulation of Body-Mass Index / Metabolic Pathways

Introduction

Global warming induces a genomic change in humans. Global warming induces endosymbiotic archaeal and RNA viroidal growth. The porphyrins form a template for the formation of RNA viroids, DNA viroids, prions, isoprenoids and polysaccharides. They can symbiose together to form primitive archaea. The archaea can further induce HIF alpha, aldose reductose and fructolysis resulting in further porphyrinogenesis and archaeal self replication. The primitive archaeal DNA is integrated along with RNA viroids which are converted to their corresponding DNA by the action of redox stress induced HERV reverse transcriptase into the human genome by the redox stress induced HERV integrase. The archaeal DNA sequences that are integrated into the human genome forms endogenous archaeal human genomic sequences akin to HERV sequences and can function as jumping genes regulating genomic DNA flexibility. The integrated endogenous genomic archaeal sequences can get expressed in the presence of redox stress forming endosymbiotic archaeal particles which can function as a new organelle called the archaeaons. The archaeaon can express the fructolytic pathway constituting an organelle called the fructosome, cholesterol catabolic pathway and digoxin synthetic forming an organelle called the steroidelle, the shikimic acid pathway forming an organelle called the neurotransminoid, antioxidant vitamin E and vitamin C synthetic organelle called the vitaminocyte as well as the glycosaminoglycan synthetic organelle called glycosaminoglycoid. The archaeaon secreting RNA viroids is called the viroidelle.

The increase in endogenous EDLF, a potent inhibitor of membrane Na^+-K^+ ATPase, can decrease this enzyme activity. The results showed increased endogenous EDLF synthesis as evidenced by increased HMG CoA reductase activity, which functions as the rate limiting step of the isoprenoid pathway.

Studies in our laboratory have demonstrated that EDLF is synthesized by the isoprenoid pathway. The endosymbiotic archaeal sequences in the human genome get expressed by redox stress and osmotic stress of global warming. This results in induction of HIF alpha which will upregulate fructolysis and glycolysis. In the setting of redox stress all glucose gets converted to fructose by the induction of enzymes aldose reductase and sorbitol dehydrogenase. Aldose reductase converts glucose to sorbitol and sorbitol dehydrogenase converts sorbitol to fructose. Since fructose is preferentially phosphorylated by ketohexokinases the cell is depleted of ATP and glucose phosphorylation comes to a halt. Fructose becomes the dominant sugar that is metabolized by fructolysis in expressed archaeal particles in the cell functioning as organelle called fructosoids. The fructose is phosphorylated to fructose 1-phosphate which is acted upon by aldolase B which converts it into glyceraldehyde 3-phosphate and dihydroxy acetone phosphate. Glyceraldehyde 3-phosphate is converted to D1,3-biphosphoglycerate which is then converted to 3-phosphoglycerate. The 3-phosphglycerate is converted to 2-phosphoglycerate. 2-phosphoglycerate is converted to phosphoenol pyruvate by the enzyme enolase. Phosphoenol pyruvate is converted to pyruvate by the enzyme pyruvic kinase. The archaeaon induces HIF alpha which upregulates fructolysis and glycolysis but inhibits pyruvate dehydrogenase. The forward metabolism of pyruvate is stopped. The dephosphorylation of phosphoenol pyruvate is inhibited in the setting of pyruvic kinase inhibition. Phosphoenol pyruvate enters the shikimic acid pathway where it is converted to chorismate. The shikimic acid is synthesized by a pathway starting from glyceraldhyde 3-phosphate. Glyceraldehyde 3-phosphate combines with the pentose phosphate pathway metabolite sedoheptulose 7-phosphate which is converted to erythrose 4-phosphate. The pentose phosphate pathway is upregulated in the presence of the suppression of glycolytic pathway. Erythrose 4-phosphate combines with

phosphoenol pyruvate to generate shikimic acid. Shikimic acid combines with another molecule of phosphoenol pyruvate to generate chorismate. The chorismate is converted to prephenic acid and then to parahydroxy phenyl pyruvic acid. Parahydroxy phenyl pyruvic acid is converted to tyrosine and tryptophan as well as neuroactive alkaloids. The shikimic acid pathway is structured in expressed archaeaon organelle called the neurotransminoid. The fructolytic intermediates glyceraldehydes 3-phosphate and pyruvate are the starting points of the DXP pathway of cholesterol synthesis. Glyceraldehyde 3-phosphate combines with pyruvate to form 1-deoxy D-xylulose phosphate (DOXP) which is then converted to 2C methyl erythritol phosphate. 2C methyl erythritol phosphate can be synthesized from erythrose 4-phosphate a metabolite of the shikimic acid pathway. DXP combines with MEP to form isopentenyl pyrophosphate which is converted to cholesterol. Cholesterol is catabolized by archaeal cholesterol oxidases to generate digoxin. The digoxin sugars digitoxose and rhamnose are synthesized by the upregulated pentose phosphate pathway. Glycolytic suppression leads to upregulation of the pentose phosphate pathway. The expressed archaeaon organelle concerned with cholesterol catabolism and digoxin synthesis is called the steroidelle. The suppression of glycolysis and stimulation of fructolysis results in upregulation of the hexosamine pathway. Fructose is converted to fructose 6-phosphate by ketohexokinases. The fructose 6-phosphate is converted to glucosamine 6-phosphate by the action of glutamine fructose 6-phosphate amidotransferase (GFAT). Glucosamine 6-phosphate is converted to UDP N-acetyl glucosamine which is then converted to N-acetyl glucosamine and various amino sugars. UDP glucose is converted to UDP D-glucuronic acid. UDP D-glucuronic acid is converted to glucuronic acid. This forms the uronic acid synthetic pathway. Uronic acids and hexosamines form repeating units of glycosaminoglycans. In the setting of glycolytic suppression and fructolytic metabolism fructolysis

leads to increase synthesis of hexosamines and GAG synthesis. The GAG synthesizing archaeaon particles are called the glycosaminoglycoids. The expressed archaeaon particles are capable of synthesizing antioxidant vitamin C and E. The UDP D-glucose is converted to UDP D-glucuronic acid. UDP D-glucuronic acid is converted to D-glucuronic acid. D-glucuronic acid is converted to L-gulonate by enzyme aldoketoreductases. L-gulonate is converted to L-gulonolactone by lactonase. L-gulonolactone is converted to ascorbic acid by the action of archaeal L-gulo oxidase. The vitamin E is synthesized from shikimate which is converted to tyrosine and then to parahydroxy phenyl pyruvic acid. Parahydroxy phenyl pyruvic acid is converted to homogentisate. Homogentisate is converted to 2-methyl 6-phytyl benzoquinone which is converted to alpha tocopherol. 2-methyl 6-phytyl benzoquinone is converted to 2,3-methyl 6-phytyl benzoquinone and gamma tocopherol. Vitamin E can also be synthesized by the DXP pathway. Glyceraldehyde 3-phosphate and pyruvate combined to form 1-deoxy D-xylulose 5-phosphate which is converted to 3-isopentenyl pyrophosphate. 3-isopentenyl pyrophosphate and dimethyl allyl pyrophosphate combined to form 2-methyl 6-phytyl benzoquinone which is converted to tocopherols. The ubiquinone another important membrane antioxidant and part of the mitochondrial electron transport chain is synthesized by the shikimic acid pathway and DXP pathway. The isoprenoid moiety of ubiquinone is contributed from the DXP pathway and the rest of it by tyrosine catabolism. The tyrosine is generated by the shikimic acid pathway. The archaeaon particles concerned with the synthesis of vitamin C, vitamin E and ubiquinone which are all antioxidants are called the vitaminocyte.

Global warming can lead to osmotic stress consequent to dehydration. The increase in actinidic archaeal growth leads to cholesterol catabolism and digoxin synthesis. Digoxin produces membrane sodium potassium ATPase inhibition and increase in intracellular calcium producing mitochondrial dysfunction. This

results in oxidative stress. The oxidative stress and osmotic stress can induce the enzyme aldose reductase which converts glucose to fructose. Fructose has got a low km value for ketokinase as compared to glucose. Therefore fructose gets phosphorylated more to fructose phosphate and the cell is depleted of ATP. The cell depletion of ATP leads to oxidative stress and chronic inflammation consequent to induction of NFKB. Oxidative stress can open the mitochondrial PT pore producing release of cyto C and activation of the caspase cascade of cell death. The fructose phosphate can enter the pentose phosphate pathway synthesizing ribose and nucleic acid. The depletion of cellular ATP results in generation of AMP and ADP which are acted upon by deaminases causing hyperuricemia. Uric acid can produce endothelial dysfunction and vascular disease. Uric acid can also produce mitochondrial dysfunction. The fructose phosphate can enter the glucosamine pathway synthesizing GAG and producing mucopolysaccharide accumulation. Fructose can fructosylate proteins making them antigenic and producing an autoimmune response. This can lead to global warming related metabolic syndrome X.

Metabolic syndrome X is associated with trunkal obesity and high body-mass index. Previous reports have shown that there is increased secretion of an endogenous digoxin like factor (EDLF) in syndrome X. EDLF is secreted by the hypothalamus and functions as the endogenous regulator of membrane sodium-potassium ATPase and synaptic neurotransmission. Studies from this laboratory have demonstrated that the EDLF is chemically the steroidal glycoside digoxin, and that it is synthesized by the isoprenoid pathway. The isoprenoid pathway also synthesizes three other metabolites important in cellular regulation - dolichol, ubiquinone and cholesterol. We have documented individuals with low body-mass index. It was therefore considered pertinent to study the isoprenoid pathway related biochemical cascade - digoxin and neurotransmitter patterns, dolichol levels and glycoconjugate metabolism and

ubiquinone levels and free radical metabolism in individuals with high and low body-mass index. Since hypothalamic archaeal digoxin can regulate neuronal transmission the isoprenoid pathway and its related cascade was assessed in individuals with right hemispheric, left hemispheric and bihemispheric dominance to find out the correlation between hemispheric dominance, metabolic status and body-mass index. Body-mass index has a close correlation with metabolic syndrome X with its related predilection for vascular thrombosis and insulin resistance (non insulin dependent diabetes mellitus). The results are discussed in this setting.

Results

(1) The results showed that plasma HMG CoA reductase activity, plasma digoxin and dolichol levels were increased and plasma ubiquinone, RBC membrane Na^+-K^+ ATPase activity and plasma magnesium reduced in individuals with high body-mass index and right hemispheric dominance. The results showed that plasma HMG CoA reductase activity, plasma digoxin and dolichol were decreased and plasma ubiquinone, RBC membrane Na^+-K^+ ATPase and plasma magnesium increased in individuals with low body-mass index left hemispheric dominance.

(2) The results showed that the concentration of tryptophan and its catabolites was found to be higher in the plasma of individuals with high body-mass index and right hemispheric dominance while that of tyrosine and its catabolites was lower. The reverse patterns were obtained in individuals with low body-mass index and left hemispheric dominance.

(3) There was increase in plasma lipid peroxidation products with decreased antioxidant protection as indicated by decrease in plasma ubiquinone and RBC reduced glutathione in individuals with high body-mass index. The activity of enzymes involved in free radical scavenging is decreased in

individuals with high body-mass index. The reverse patterns were obtained in individuals with low body-mass index.

(4) The results show an increase in the concentration of plasma total GAG and individual GAG fractions, glycolipids and carbohydrate components of glycoproteins in individuals with high body-mass index. The activity of GAG degrading enzymes and that of glycohydrolases showed significant increase in the plasma in individuals with high body-mass index. The reverse patterns were obtained in individuals with low body-mass index.

(5) The cholesterol: phospholipid ratio of the RBC membrane was increased in individuals with high body-mass index. The concentration of total GAG, hexose and fucose of glycoprotein decreased in the RBC membrane and increased in the serum in individuals with high body-mass index. The reverse patterns were obtained in individuals with low body-mass index.

Discussion

Archaeal Digoxin and Membrane Na^+-K^+ ATPase Inhibition in Relation to Body-Mass Index

The archaeaon steroidelle DXP pathway and the upregulated pentose phosphate pathway contribute to digoxin synthesis. The increase in endogenous digoxin, a potent inhibitor of membrane Na^+-K^+ ATPase, can decrease this enzyme activity in individuals with high body-mass index. In individuals with high body-mass index, there was significant inhibition of the RBC membrane Na^+-K^+ ATPase. There is increased digoxin synthesis in individuals with high body-mass index as evidenced by increased HMG CoA reductase activity. The inhibition of Na^+-K^+ ATPase by digoxin is known to cause an increase in intracellular calcium resulting from increased Na^+-Ca^{++} exchange. This increase in intracellular calcium by displacing magnesium from its binding sites causes a

decrease in the functional availability of magnesium. This decrease in the availability of magnesium can cause decreased mitochondrial ATP formation which along with low magnesium can cause further inhibition of Na^+-K^+ ATPase, since the ATP magnesium complex is the actual substrate for this reaction. There is thus a progressive inhibition of Na^+-K^+ ATPase activity first triggered by digoxin. Low intracellular magnesium and high intracellular calcium consequent to Na^+-K^+ ATPase inhibition appear to be crucial to the pathophysiology of individuals with high body-mass index. Serum magnesium was assessed in individuals with high body-mass index and was found to be reduced. This finding agrees with reports of increase EDLF activity in metabolic syndrome X with associated trunkal obesity. On the other hand in individuals with low body-mass index the reverse patterns were obtained. There was decreased digoxin synthesis and consequent stimulation of membrane Na^+-K^+ ATPase, resulting in decreased intracellular calcium / increased intracellular magnesium. Serum magnesium was elevated in individuals with low body-mass index.

Magnesium is required as a co-factor for cell membrane glucose transport. Hypomagnesemia consequent to membrane Na^+-K^+ ATPase inhibition in individuals with a high body-mass index can lead to defective cell membrane transport of glucose. Alteration in cellular membrane composition reported here can also inhibit the membrane transport of glucose. Increased intracellular calcium can activate the G-protein coupled signal transduction of the contrainsulin hormones (growth hormone and glucagon) leading to hyperglycemia. Magnesium translocation appears to be an early event in insulin action. Decrease in intracellular magnesium can block the phosphorylation reactions involved in protein tyosine kinase receptor activity leading to insulin resistance. Alteration in cell membrane composition reported here can also modulate the insulin receptor leading to insulin resistance. Decrease in

intracellular magnesium can lead to inhibition of the glycolytic pathway. Increase in intracellular calcium can open up the mitochondrial PT pore and block oxidative phosphorylation. This leads to defective glucose utilisation and contributes to the development of non-insulin dependent diabetes mellitus common in individuals with high body-mass index. Increase in beta cell calcium can contribute to increased insulin release from beta cells and hyperinsulinemia. Hyporuagnesemia has been reported to markedly increased glucose stimulated insulin secretion by the perfuse pancreas. Decreased intracellular magnesium can produce dysfunction of lipoprotein lipase, producing defective catabolism of triglycerides rich lipoproteins and hypertriglyceridemia. In hypomagnesemia lecithin cholesterol acyl transferase (LCAT) is defective and there is reduced formation of cholesterol esters in I-IDL. This results in reduced HDL cholesterol described in individuals with high body-mass index. Magnesium deficiency has been reported to increase LDL cholesterol levels also. Nicotine administration has also been reported to produce significant changes in lipid metabolism. There is increased tissue cholesterogenesis, decreased hepatic degradation of cholesterol and increased triglycerides synthesis. The uptake of circulating triglyceride rich lipoprotein is decreased as revealed by decreased activity of extra hepatic lipoprotein lipase. Plasma LCAT activity is also reduced on nicotine administration. HDL cholesterol is decreased while the LDL-VLDL cholesterol is increased. The absence of morphine in individuals with high body-mass index is also significant. Morphine has been reported to have an effect on glucose metabolism by increasing glucagon Secretion, modulating insulin release from the beta cell and independently through opioid / alphaadrenergic receptors stimulation. These patterns are reversed in individuals with low body-mass index. In individuals with low body-mass index intracellular hypermagnesemia consequent to membrane sodium potassium ATPase stimulation can promote

glucose transport into the cell, increase the activity of the insulin receptor, promote mitochondrial oxidative phosphorylation and increase glucose utilisation. Increase in intracellular magnesium can promote lipoprotein lipase activity promoting triglyceride catabolism and increase the efficiency of mitochondrial beta oxidation of fatty acids. The LCAT activity and HMG CoA reductase activity and cholesterol synthesis are also decreased in intracellular hypermagnesemia. Increase in morphine levels in individuals with low body-mass index can promote glucose utilisation. Thus membrane Na^+-K^+ ATPase activity can modulate the insulin receptor activity and influence lipid and carbohydrate metabolism important in the regulation of body-mass index. Membrane Na^+-K^+ ATPase activity can also modulate the intracellular magnesium / calcium concentration within the vascular smooth muscle cell. In individuals with high body-mass index membrane Na^+-K^+ ATPase inhibition can lead to depletion of intracellular magnesium contributing to vasospasm. Increase in intracellular calcium can increase the G-protein coupled activity of platelet activating factor and thrombin receptor contributing to thrombosis. This could relate membrane Na^+-K^+ ATPase inhibition and high body-mass index with vascular thrombosis. The reverse holds good for low body-mass index where there is a decreased predilection for vascular thrombosis.

Archaeal Digoxin and Regulation of Neurotransmitter Synthesis and Function in Relation to Body-Mass Index

The archaeaon neurotransminoid shikimic acid pathway contributes to tryptophan and tyrosine synthesis and catabolism generating neurotransmitters and neuroactive alkaloids. There is an increase in tryptophan and its catabolites and a reduction in tyrosine and its catabolites in the plasma of individuals with high body-mass index which could be due to the fact that digoxin can regulate the neutral amino acid transport system with preferential promotion of

tryptophan transport over tyrosine. The decrease in membrane Na^+-K^+ ATPase activity in individuals with high body-mass index could be due to the fact that the hyperpolarising neurotransmitters (dopamine morphine and noradrenaline) are reduced and the depolarising neuroactive compounds (serotonin, strychnine, nicotine and quinolinic acid) are increased. The schizoid neurotransmitter pattern of reduced dopamine, noradrenaline and morphine and increased serotonin, strychnine and nicotine is common to individuals with high body-mass index and schizophrenia and could predispose to its development. In the presence of hypomagnesmia, the magnesium block on the NMDA receptor is removed leading to NMDA excitotoxicity. Thus in individuals with a high body-mass index with a hyperdigoxinemic state there is upregulated serotoninergic, cholinergic and glutamatergic transmission and downregulated dopaminergic, glycinergic and noradrenergic transmission. On the other hand the reverse patterns were obtained in patients with low body-mass index with a hypodigoxinemia induced increase in tyrosine catabolites over tryptophan contributing to membrane Na^+-K^+ ATPase stimulation. Hypermagnesemia could also inhibit NMDA transmission. Low serotonin is associated with psychological states of depression and obsessive compulsive disorder which could predispose to the development of low body-mass index. Thus in the low body-mass index state there is upregulated dopaminergic, noradrenergic, morphinergic transmission and down regulated serotoninergic, cholinergic and glutamatergic transmission. There are no previous reports correlating body-mass index with neurotransmitter patterns.

Archaeal Digoxin and Regulation of Golgi Body / Lysosomal Function in Relation to Body-Mass Index

The archaeaon glycosaminoglycoid and fructosoid contributes to glycoconjugate synthesis and catabolism by the process of fructolysis. The

elevation in the level of dolichol in individuals with high body-mass index may suggest its increased availability of N-glycosylation of proteins. Magnesium deficiency has been reported to upregulate glycosaminoglycan and glycolipid synthesis. The increase in the activity of glycohydrolases and GAG degrading enzymes could be due to reduced lysosomal stability and consequent leakage of lysosomal enzymes into the serum. The increase in the concentration of carbohydrate components of glycoproteins and GAG inspite of increased activity of many glycohydrolases may be due to their possible resistance to cleavage by glycohydrolases consequent to qualitative change in their structure. Increased accumulation of glycoconjugates in the vascular wall due to defective catabolism can lead to atherosclerosis common in metabolic syndrome X. The opposite patterns, with decreased dolichol and hypermagnesemia inhibiting glycoconjugate synthesis are noticed in individuals with low body-mass index. The decrease in the activity of glycohydrolases and GAG degrading enzymes could be due to increased lysosomal stability. Decreased glycoconjugate levels in the arterial wall can possibly lead to decreased incidence of atherosclerosis. This could relate body-mass index to vascular disease.

Archaeal Digoxin and Alteration in Membrane Structure and Membrane Formation in Relation to Body-Mass Index

The archaeaon steroidelle, glycosaminoglycoid and fructosoid contribute to cell membrane formation synthesizing cholesterol by the DXP pathway and glycosaminoglycans by fructolysis. The upregulation of the isoprenoid pathway in individuals with high body-mass index can lead to increased cholesterol synthesis and magnesium deficiency can inhibit phospholipid synthesis leading to increased membrane cholesterol: phospholipid ratio. The concentration of total GAG, hexose and fucose content of glycoprotein decreased in the RBC membrane and increased in the plasma suggesting their reduced incorporation

into the membrane and defective membrane formation. This is a consequence of defective membrane trafficking which depends upon GTPases and lipid kinases requiring magnesium as a cofactor and are defective in magnesium deficiency. The change in membrane structure produced by alteration in glycoconjugates and the cholesterol: phospholipid ratio can produce changes in the conformation of Na^+-K^+ ATPase resulting in further membrane Na^+-K^+ ATPase inhibition. The same changes can affect the structure of the organelle membrane contributing to defective lysosomal stability. The opposite patterns with hypermagnesemia induced decreased cholesterol synthesis, increased phospholipid synthesis and decreased membrane cholesterol: phospholipid ratio are noticed in individuals with low body-mass index. Also the membrane glycoconjugates are increased and plasma glycoconjugates decreased owing to increased activity of trafficking enzymes consequent to hypermagnesemia. This leads to further membrane Na^+-K^+ ATPase stimulation and increased lysosomal stability in individuals with low body-mass index. Alteration in membrane structure can affect the transport of glucose into the cell as well as modulate the function of the insulin receptor contributing insulin resistance. There are no previous reports relating alterations in connective tissue metabolism and membrane formation to body-mass index. Not only is there increased adiposity in individuals with high body-mass index, there is also increased volume of connective tissue and intercellular matrix in this group of individuals.

Archaeal Digoxin and Mitochondrial Dysfunction in Relation to Body-Mass Index

The archaeaon vitaminocyte contributes to the synthesis of ubiquinone and mitochondrial electron transport chain function. The mitochondrial function related free radical generation is regulated by the archaeaon vitaminocyte synthesized tocopherol and ascorbic acid. The concentration of ubiquinone

decreased significantly in individuals with high body-mass index which may be the result of low tyrosine levels, reported in individuals with low body-mass index, consequent to digoxin's effect in preferentially promoting tryptophan transport over tyrosine. The aromatic ring portion of ubiquinone is derived from tyrosine. Ubiquinone is an important component of the mitochondrial electron transport chain, and its deficiency leads to mitochondrial oxidative phosphorylation defects. The increase in intracellular calcium can open the mitochondrial PT pore causing a collapse of the hydrogen gradient across the inner membrane and uncoupling of the respiratory chain. Intracellular magnesium deficiency can lead to a defect in the function of ATP synthase. All this leads to defects in mitochondrial oxidative phosphorylation, incomplete reduction of oxygen and generation of the superoxide ion which produces lipid peroxidation. The increase in intracellular calcium may lead to increased generation of NO by inducing the enzyme nitric oxide synthase which combines with the superoxide radical to form peroxynitrite. Ubiquinone deficiency also leads to reduced free radical scavenging. Magnesium deficiency can affect glutathione synthetase arid glutathione reductase function. The mitochondrial superoxide dismutase leaks out and becomes dysfunctional with calcium related opening of the mitochondrial PT pore and outer membrane rupture. The peroxisomal membrane is defective owing to a membrane Na^+-K^+ ATPase inhibition related defect in membrane formation and leads to reduced catalase activity. Increased generation of free radicals like the superoxide ion and hydroxyl radical can produce lipid peroxidation and cell membrane damage which can further inactivate Na^+-K^+ ATPase, triggering the cycle of free radical generation once again. Thus there is decreased efficiency of mitochondrial oxidative phosphorylation in individuals with high body-mass index. Increased generation of free radicals can oxidise LDL contributing to atherosclerosis described in metabolic syndrome X and individuals with high body-mass index. The patterns are reversed in individuals with low body-mass index. The

concentration of ubiquinone increased significantly in individuals with low body-mass index which may be the result of increased tyrosine levels, consequent to digoxin deficiency. The decrease in intracellular calcium can stabilise the mitochondrial PT pore and intracellular hypermagnesemia can increase the activity of ATPase synthase leading on to improved mitochondrial function and reduced free radical generation. The decrease in intracellular calcium may lead to decreased generation of NO by inhibiting the enzyme nitric oxide synthase and reduced peroxynitrite formation. Ubiquinone excess also leads to increased free radical scavenging. The perxoxisomal membrane is stabilised leading to increased catalase activity. The activity of mitochondrial superoxide dismutase is made more efficient owing to stabilisation of the mitochondrial PT pore. In the presence of intracellular hypermagnesemia consequent to membrane sodium-potassium ATPase stimulation the activity of glutathione synthetase and glutathione reductase is upregulated. Decreased generation of free radicals like the superoxide ion and hydroxyl radical can stabilise the cell membrane and further stimulate membrane Na^{+}-K^{+} ATPase. Thus there is increased efficiency of mitochondrial oxidative phosphorylation in individuals with low body-mass index. This can lead to decreased generation of free radicals and inhibition of LDL oxidation resulting in a decreased incidence of vascular disease. There are no previous reports correlating altered mitochondrial function and ubiquinone synthesis with body-mass index. Alteration in mitochondrial function and glucose utilisation could contribute to the body-mass index of the individual. It would also have a relation to the incidence of vascular thrombosis.

Archaeal Digoxin and Hemispheric Dominance in Relation to Body-Mass Index

The archaeaon related organelle-steroidelle, neurotransminoid and vitaminocyte contribute to hemispheric dominance. The biochemical pattern in

individuals with a high body-mass index correlated well with right hemispheric dominance. Right hemispheric dominance is associated with an upregulated isoprenoid pathway and hyperdigoxinemia. The biochemical patterns in individuals with a low body-mass index correlated well with left hemispheric dominance. Left hemispheric dominance is associated with a downregulated isoprenoid pathway and hypodigoxinemia. Hemispheric dominance may play a vital role in determining body-mass index, metabolic status and risk for vascular thrombosis. It could also modulate insulin resistance and development of non insulin dependent diabetes mellitus. There are no previous reports relating hemispheric dominance to metabolic syndrome X.

Thus body-mass index depends on hemispheric dominance and alterations in the isoprenoid pathway. In individuals with high body-mass index there is chemical right hemispheric dominance with an upregulated isoprenoid pathway, hyperdigoxinemia, increased tryptophan catabolism over tyrosine, increased glycoconjugate synthesis, reduced lysosomal stability and decreased efficiency of mitochondrial oxidative phosphorylation. In individuals with low body-mass index there is chemical left hemispheric dominance with a downregulated isoprenoid pathway, hypodigoxinemia, decreased tryptophan catabolism over tyrosine, decreased glycoconjugate synthesis, increased lysosomal stability and increased efficiency of mitochondrial oxidative phosphorylation.

References

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