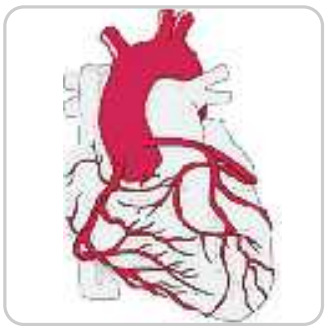
The Ontogeny of Metabolic Syndrome

Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke - Human Atavistic Archaeal Colonies with Neanderthal Metabolonomics

Ravikumar Kurup and Parameswara Achutha Kurup



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Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke – Human Atavistic Archaeal Colonies with Neanderthal Metabolonomics

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A Cholesterol and Actinide Dependent Shadow Biosphere of Archaea and Viroids in Metabolic Syndrome-Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke

Introduction

Actinides like rutile, endogenous digoxin as well as organisms like phytoplasmas and viroids have been implicated in the etiology of metabolic syndrome x-type 2 diabetes mellitus, CVA and CAD[1-4]. Endogenous digoxin has been related to the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[4]. The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered[5-8]. An actinide dependent shadow biosphere of archaea and viroids in metabolic syndrome x, CVA and CAD is described[7, 9]. Metal actinides in beach sands have been postulated to play a role in abiogenesis[7]. A hypothesis of cholesterol as the primal prebiotic molecule synthesized on actinide surfaces with all other biomolecules arising from it and a self replicating cholesterol lipid organism as the initial life form is presented.

Materials and Methods

The following groups were included in the study: – metabolic syndrome x-type 2 diabetes mellitus, CVA and CAD. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond[10]. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for

1 hour. The following estimations were carried out: – Cytochrome F420, free RNA, free DNA, polycyclic aromatic hydrocarbon, hydrogen peroxide, dopamine, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids[11-13]. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Polycyclic aromatic hydrocarbon was estimated by measuring hydrogen peroxide liberated by using glucose reagent. Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-7 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1 *Effect of rutile and antibiotics on cytochrome F420 and PAH.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66	4.45	0.14	18.25	0.72
DM	22.59	1.86	57.05	8.45	23.40	1.55	65.77	5.27
CVA	22.29	1.66	59.02	7.50	23.23	1.97	65.89	5.05
CAD	22.06	1.61	57.81	6.04	23.46	1.91	61.56	4.61
	F value 306.749 P value < 0.001		F value 130.054 P value < 0.001		F value 391.318 P value < 0.001		F value 257.996 P value < 0.001	

Table 2 *Effect of rutile and antibiotics on free RNA and DNA.*

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy+Cipro)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
DM	23.01	1.67	65.35	3.56	23.33	1.86	66.46	3.65
CVA	22.56	2.46	62.70	4.53	23.32	1.74	65.67	4.16
CAD	23.30	1.42	65.07	4.95	23.11	1.52	66.68	3.97
	F value 337.577 P value < 0.001		F value 356.621 P value < 0.001		F value 427.828 P value < 0.001		F value 654.453 P value < 0.001	

Table 3 *Effect of rutile and antibiotics on HMG CoA reductase and ATP synthase.*

Group	HMG CoA R % change (Increase with Rutile)		HMG CoA R % change (Decrease with Doxy+Cipro)		ATP synthase % (Increase with Rutile)		ATP synthase % (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.30	0.20	18.35	0.35	4.40	0.11	18.78	0.11
DM	23.06	1.65	62.25	6.24	23.72	1.73	66.25	3.69
CVA	22.86	2.58	66.53	5.59	23.15	1.62	66.48	4.17
CAD	22.38	2.38	60.65	5.27	23.00	1.64	66.67	4.21
	F value 319.332 P value < 0.001		F value 199.553 P value < 0.001		F value 449.503 P value < 0.001		F value 673.081 P value < 0.001	

Table 4 *Effect of rutile and antibiotics on digoxin and bile acids.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		Bile acids % change (Increase with Rutile)		Bile acids % change (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	0.11	0.00	0.054	0.003	4.29	0.18	18.15	0.58
DM	0.47	0.04	0.202	0.025	22.87	2.58	64.51	5.93
CVA	0.56	0.05	0.220	0.052	22.29	1.47	64.35	5.58
CAD	0.53	0.06	0.212	0.045	23.30	1.88	62.49	7.26
	F value 135.116 P value < 0.001		F value 71.706 P value < 0.001		F value 290.441 P value < 0.001		F value 203.651 P value < 0.001	

Table 5 *Effect of rutile and antibiotics on pyruvate and hexokinase.*

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy+Cipro)		Hexokinase % change (Increase with Rutile)		Hexokinase % change (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.34	0.21	18.43	0.82	4.21	0.16	18.56	0.76
DM	20.67	1.38	58.75	8.12	23.23	1.88	65.11	5.14
CVA	21.21	2.36	58.73	8.10	21.11	2.25	64.20	5.38
CAD	21.07	1.79	63.90	7.13	22.47	2.17	65.97	4.62
	F value 321.255 P value < 0.001		F value 115.242 P value < 0.001		F value 292.065 P value < 0.001		F value 317.966 P value < 0.001	

Table 6 *Effect of rutile and antibiotics on hydrogen peroxide and delta amino levulinic acid.*

Group	H_2O_2 % (Increase with Rutile)		H_2O_2 % (Decrease with Doxy+Cipro)		ALA % (Increase with Rutile)		ALA % (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.43	0.19	18.13	0.63	4.40	0.10	18.48	0.39
DM	23.27	1.53	58.91	6.09	22.87	1.84	66.31	3.68
CVA	23.32	1.71	63.15	7.62	23.45	1.79	66.32	3.63
CAD	22.86	1.91	63.66	6.88	23.17	1.88	68.53	2.65
	F value 380.721 P value < 0.001		F value 171.228 P value < 0.001		F value 372.716 P value < 0.001		F value 556.411 P value < 0.001	

Table 7 *Effect of rutile and antibiotics on dopamine and serotonin.*

Group	DOPAMINE % (Increase with Rutile)		DOPAMINE % (Decrease with Doxy+Cipro)		5 HT % change (Increase with Rutile)		5 HT % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.41	0.15	18.63	0.12	4.34	0.15	18.24	0.37
DM	24.10	1.61	65.78	4.43	22.73	2.46	65.87	4.35
CVA	23.43	1.57	66.30	3.57	22.98	1.50	65.13	4.87
CAD	23.70	1.75	68.06	3.52	23.81	1.49	64.89	6.01
	F value 403.394 P value < 0.001		F value 680.284 P value < 0.001		F value 348.867 P value < 0.001		F value 364.999 P value < 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[6, 14]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[15]. There was also an increase in archaeal HMG CoA reductase activity indicating increased cholesterol synthesis by the archaeal mevalonate pathway. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis and archaeal cholesterol hydroxylase activity indicating bile acid synthesis were increased[8]. The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide[14]. The pyruvate gets converted to glutamate and ammonia by the GABA shunt pathway. The archaeal aromatization of cholesterol generating PAH, serotonin and dopamine was also detected[16]. The archaeal glycolytic hexokinase activity and archaeal extracellular ATP synthase activity were increased. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[17]. There was an

increase in free RNA indicating self replicating RNA viroids and free DNA indicating generation of viroid complementary DNA strands by archaeal reverse transcriptase activity. The actinides modulate RNA folding and catalyse its ribozymal action. Digoxin can cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities[18]. Archaeal pyruvate can produce histone deacetylase inhibition resulting in endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the RNA viroidal complementary DNA into the noncoding region of eukaryotic non coding DNA using HERV integrase as has been described for borna and ebola viruses[19]. The noncoding DNA is lengthened by integrating RNA viroidal complementary DNA with the integration going on as a continuing event. The archaea genome can also get integrated into human genome using integrase as has been described for trypanosomes[20]. The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites[19, 20]. This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters as well as eukaryotic speciation and individuality[21]. The viroidal complementary DNA can function as jumping genes producing a dynamic genome important in storage of synaptic information, HLA gene expression and developmental gene expression. The RNA viroids can regulate mRNA function by RNA interference[18]. The phenomena of RNA interference can modulate T cell and B cell function, insulin signaling lipid metabolism, cell growth and differentiation, apoptosis, neuronal transmission and euchromatin/ heterochromatin expression. This contributes to the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

Archaea and RNA viroid can bind the TLR receptor induce NFKB producing immune activation and cytokine TNF alpha secretion. The archaeal DXP and

mevalonate pathway metabolites can bind γδ TCR and digoxin induced calcium signaling can activate NFKB producing chronic immune activation[4, 23]. The archaea and viroid induced chronic immune activation and generation of superantigens can lead on to autoimmunity in metabolic syndrome x, CVA and CAD. Archaea, viroids and digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype[24]. The increased glycolytic hexokinase activity, decrease in blood ATP, leakage of cytochrome C, increase in serum pyruvate and decrease in acetyl CoA indicates the generation of the Warburg phenotype. There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics and metabolic syndrome. The archaea and viroid generated cytokines can lead to TNF alpha induced insulin resistance and Metabolic Syndrome-type 2 diabetes mellitus with CAD and CVA. The accumulated pyruvate enters the GABA shunt pathway and is converted to citrate which is acted upon by citrate lyase and converted to acetyl CoA, used for cholesterol synthesis[24]. The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy needs. The increased cholesterol substrate leads to increased archaeal growth and digoxin synthesis leading to metabolic channeling to the mevalonate pathway. The archaeal bile acids are steroidal hormones which can bind GPCR and modulate D2 regulating the conversion of T4 to T3 which activates uncoupling proteins, can activate NRF ½ inducing NQO1, GST, HOI reducing redox stress, can bind FXR regulating insulin receptor sensitivity and bind PXR inducing the bile acid shunt pathway of cholesterol detoxification[25]. The archaea and viroid induced monocyte activation and Warburg phenotype induced increased cholesterol synthesis leads to atherogenesis. The RNA viroids can recombine with HERV sequences and get encapsulated in microvesicles contributing to the retroviral state. The prion protein conformation is modulated by RNA viroid binding producing Prion Disease. Prion proteins and HERV sequences are related to

metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[4]. Thus the archaea and the viroids are crucial to the etiopathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

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The Archaeal Induced Stem Cell Conversion Produces an Epidemic Benjamin Buttons Reverse Aging Syndrome Leading to Metabolic Syndrome-Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke

Introduction

The global warming produces increased acidity and atmospheric carbon dioxide resulting in extremophilic archaeal symbiosis in humans. The archaeal symbiosis results in neanderthalisation of humans. The archaea induced uncoupling proteins producing the primitive Warburg phenotype and stem cell metabolonomics. The archaeal metabolites of cholesterol digoxin, bile acids and short chain fatty acids induce uncoupling proteins. The lysosomal enzymes a marker of stem cell conversion are markedly increased along with genesis of the archaeal phenotype in metabolic syndrome-type 2 diabetes mellitus with coronary artery disease and stroke. In metabolic syndrome-type 2 diabetes mellitus with CAD and CVA there is somatic cell transformation to stem cell and lose of function. The neurons become immature and lose their dendritic spines and connectivity. This results in loss of neuronal function and reversion to archaeal magnetite mediated extrasensory perception of low level of EMF. Exposure to low level of EMF results in brain changes. This results in prefrontal cortex atrophy. The primitive brain areas of cerebellum and brain stem become hypertrophic. The somatic and neuronal cell proliferates and there is neanderthalisation of the brain and body. Prefrontal lobe function needs dynamic synaptic connectivity which is produced by jumping genes mediated by human endogenous retroviral sequences. The cerebellum is the site of impulsive behavior and the unconscious behavior. The cerebellar and subcortical brain connections are predominantly archaeal colony networks. The global warming and exposure to low level of EMF leads to actinidic archaeal growth in the brain and increased archaeal magnetite mediated perception of low level of EMF. This leads to prefrontal cortex atrophy and cerebellar dominance. The conscious becomes minimal and unconscious brain takes over.

The study assessed archaeal growth as assessed by cytochrome F420 activity and stem cell type metabolonomics in metabolic syndrome-type 2 diabetes mellitus with coronary artery disease and stroke[1-17]. The results are presented in this paper.

Materials and Methods

The blood samples were also drawn from 15 cases each of metabolic syndrome-type 2 diabetes mellitus, cerebrovascular thrombosis and coronary artery diseases. The estimations done in the blood samples collected include cytochrome F420 activity. Blood lactate, pyruvate, hexokinase, cytochrome C, cytochrome F420, digoxin, bile acids, butyrate and propionate were estimated.

Results

The blood samples of metabolic syndrome x, CVA and CAD had increased blood lactate and pyruvate, increased RBC hexokinase, increased serum cytochrome C and serum cytochrome F420, increased serum digoxin, bile acids, butyrate and propionate. The metabolic syndrome x had increased cytochrome F420 activity. The serum cytochrome C levels in the blood were increased. This suggested mitochondrial dysfunction. There was an increased in glycolysis as suggested by increased RBC hexokinase activity and lactic acidosis. Owing to the mitochondrial dysfunction and pyruvate dehydrogenase inhibition there was pyruvate accumulation. The pyruvate was converted to lactate by the Cori cycle and also to glutamate and ammonia. This metabolism is suggestive of the Warburg phenotype and stem cell conversion. The stem cells depend on Warburg anaerobic glycolysis for energetics and have a mitochondrial dysfunction. The lysosomal enzyme beta galactosidase activity was increased in

the metabolic syndrome x, CVA and CAD suggesting stem cell conversion. This suggests that metabolic syndrome x, CVA and CAD tend to have stem cell metabolonomics and stem cell conversion.

Table 1

Group	Cytochrome F 420		Serum Cyto C (ng/ml)		Lactate (mg/dl)		Pyruvate (umol/l)		RBC Hexokinase (ug glu phos/hr/mgpro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal population	1.00	0.00	2.79	0.28	7.38	0.31	40.51	1.42	1.66	0.45
DM	4.00	0.00	12.95	0.56	25.56	7.93	96.30	10.33	7.05	1.86
CAD	4.00	0.00	11.51	0.47	22.83	0.82	97.29	12.45	8.88	3.09
CVA	4.00	0.00	12.74	0.80	23.03	1.26	103.25	9.49	7.87	2.72
Low level background radiation	4.00	0.00	12.26	1.00	23.31	1.46	103.28	11.47	7.58	3.09
F value	0.001		445.772		162.945		154.701		18.187	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Table 2

Group	ACOA (mg/dl)		Glutamate (mg/dl)		Se. ammonia (ug/dl)		RBC digoxin (ng/ml RBC Susp)		Beta galactosidase activity in serum (IU/ml)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal population	8.75	0.38	0.65	0.03	50.60	1.42	0.58	0.07	17.75	0.72
DM	2.17	0.40	3.53	0.44	93.38	7.76	1.35	0.26	51.98	5.05
CAD	2.37	0.44	3.61	0.28	93.93	4.86	1.22	0.16	50.00	5.91
CVA	2.25	0.44	3.31	0.43	103.18	27.27	1.33	0.27	51.06	4.83
Low level background radiation	2.14	0.19	3.47	0.37	102.62	26.54	1.41	0.30	51.01	4.77
F value	1871.04		200.702		61.645		60.288		194.418	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Discussion

The metabolic syndrome x, CVA and CAD tend to have a predominant anaerobic glycolytic metabolism and mitochondrial oxidative phosphorylation is suppressed. The metabolism is similar to the metabolism of the stem cell. The pyruvate and lactate levels are increased with a decrease in acetyl coenzyme A and ATP. The glycolytic pathway and hexokinase is increased. This indicates a Warburg phenotype depending upon anaerobic glycolysis for energetics. The lysosomal enzymes beta galactosidase a stem cell marker is increased. The cytochrome F420 is also increased as well as the archaeal catabolite digoxin which suppresses sodium potassium ATPase. Bacteria and archaea are supposed to induce stem cell transformation. The induction of uncoupling proteins leads to stem cell transformation. The uncoupling proteins inhibit oxidative phosphorylation and the substrates are directed to anaerobic glycolysis. Digoxin by inhibiting sodium potassium ATPase can increase intracellular calcium, induce mitochondrial permeability transient pore function and uncouple oxidative phosphorylation. The side chain of cholesterol is catabolised by archaea to butyric acid and propionic acid which uncouple oxidative phosphorylation. The archaeal side chain hydroxylase convert cholesterol to bile acids which uncouple oxidative phosphorylation. Thus archaeal symbiosis in the cell results in cholesterol catabolism and the catabolites digoxin, bile acids and short chain fatty acids uncouple oxidative phosphorylation, inhibit mitochondrial function and promote anaerobic glycolysis. The conversion of somatic cells to stem cell helps in archaeal persistence within the cell and symbiosis. Mycobacterium leprae infection can convert Schwann cells to stem cells. Archaeal infection produces somatic cell conversion to stem cells for archaeal persistence. The conversion to stem cell results in proliferation and loss of function resulting in metabolic syndrome-type 2 diabetes mellitus, CVA and

CAD. Stem cell conversion of neurons and loss of function results in development of a new psychological phenotype[1-17].

The systemic and neuronal cell in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD behaves like the stem cell. It is plausible to hypothesise a somatic cell conversion to stem cell in these disorders. The differentiated cells by archaeal induction get converted to stem cell. The stem cell is a immature cell with loss of function. The neurons lose their dendritic spines and loss of connectivity. The brain function becomes primitive. The neurons are adendritic and disconnected. This results in complex brain structures like the modern cerebral cortex and prefrontal cortex atrophy. The primitive parts of the brain the brain stem and cerebellum hypertrophies. This results in neanderthalisation of the brain with a prominent occipital bun and atrophied prefrontal cortex. The prefrontal cortex atrophy results in loss of logic, judgment, reasoning and executive functions. The hypertrophy of the cerebellum and brain stem results in dominance of impulsive behavior. The world of the unconscious brain with its archetypes takes over. There is loss of the world of reasoning, logic and judgment. It is a world of impulsiveness in which primitive tendencies with relation to the unconscious becomes dominant. There is inhibition of the conscious due to loss of cortical functions and the dominance of the unconscious. The increased archaeal induced proliferation of stem cells results in a big sized brain and trunk as in Neanderthals. This archaeal symbiosis produces neanderthalisation and a stem cell syndrome. This produces reverse aging which can be called as an epidemic Benjamin Button syndrome. The stem cell metabolonomics with inhibited mitochondrial function and anaerobic glycolysis results in metabolic syndrome-type 2 diabetes mellitus with CAD and CVA. The diabetic metabolism is akin to stem cell metabolism[1-17].

The cerebral cortical function requires synaptic plasticity and is modulated by HERV mediated jumping genes. This needs a dynamic brain and the human

cerebral cortex evolved due to the jumping genes generated from human endogenous retroviral sequences. The cerebellar world is mediated by the archaeal colony network. The stem cell transformation of somatic cells results in HERV resistance and retroviral resistance. Archaeal digoxin inhibits reverse transcriptase by producing magnesium deficiency as well as modulates RNA viral editing inhibiting retroviral replication. This produces lack of HERV jumping genes in this stem cell brain and lack of synaptic plasticity and dynamicity. The stem cell syndrome is characterized by retroviral resistance. Archaeal symbiosis inhibits retroviral infection. The homo sapiens with less of archaeal symbiosis becomes susceptible to retroviral and other RNA viral infection and gets wiped out. The homo neoneanderthalis are resistance to retroviral and other RNA viral infection and persists. The homo neoneanderthalis dominates all over the world. But the homo neoneanderthalis are prone to civilisational disease like metabolic syndrome-type 2 diabetes mellitus, CVA and CAD The homo neoneanderthalis becomes extinct after a period of time[1-17].

The archaeal induced stem cell syndrome or neanderthalisation is due to global warming and acid rains resulting in increased extremophilic archaeal symbiosis. The archaea catabolises cholesterol and generates digoxin, bile acids and short chain fatty acids which produce induction of uncoupling proteins. This produces mitochondrial dysfunction and the cell obtains its energetics from glycolysis. Archaeal digoxin produces membrane sodium potassium ATPase inhibition which also contributes to stem cell conversion. The whole body somatic and brain undergoes stem cell conversion and becomes a stem cell phenotype with Warburg metabolic phenotype. The generalized acidity due to global warming and increased atmospheric carbon dioxide also facilitates archaeal growth and stem cell transformation. The acidic pH due to the Warburg phenotype and increased atmospheric carbon dioxide also results in stem cell conversion. The somatic differentiated cell getting converted to stem

cells lose their function and become dysfunctional metabolically, neurologically, immunologically and endocrine-wise. This produces the epidemic Benjamin button syndrome and the human species becomes neanderthalic and a collection of immature stem cells. This results in epidemic metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The brain becomes converted to a collection of stem cells which are dedifferentiated with loss of function and is like an archaeal colony network. The perception becomes extrasensory and quantal depending on archaeal magnetite. The increased amount of low level EMF perception results in prefrontal cortical atrophy. It also produces cerebellar hypertrophy and the cerebellar cognitive function takes over. This can lead to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[1-17].

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Metabolic Syndrome-Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke – Relation to Archaeal Mediated RNA Viroids and Amyloidosis

Introduction

Prion proteins have been implicated in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The islet cell associated amyloid in diabetes mellitus is a prion protein. Prion diseases are conformational diseases. The abnormal prion protein seeded into the system converts the normal proteins with prion like domains to abnormal configuration. This abnormal protein resists digestion by lysosomal enzymes after its half life is over and results in deposition of amyloid plaques. This produces organ dysfunction. Ribonucleoproteins are well known to behave like prion proteins and form amyloid. We have demonstrated actinidic archaea which secretes RNA viroids in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The RNA viroids can bind with normal proteins with prion like domains eg., superoxide dismutase and produce a ribonucleoprotein resulting in prion phenomena and amyloidogenesis. The actinidic archaeal growth results in increased digoxin synthesis and phenotypic conversion of homo sapiens to homo Neanderthals as reported earlier. The increased actinidic archaeal growth is due to global warming and this results in neanderthalisation. Homo neanderthalis tend to have more of civilisational diseases like metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Actinidic archaeal secreted RNA viroids may play a crucial role in amyloid formation and pathogenesis of these disorders[1-16].

Materials and Methods

The following groups were included in the study: – metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the

general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+cerium 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420, free RNA, Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of cerium increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of cerium increased their levels but the extent of change was more in patient's sera as compared to controls.

Results

The results show that there was increase in cytochrome F420 in CJD and other disease groups indicating increased archaeal growth. There was also an increase in free RNA indicating self replicating RNA viroids in CJD and other disease groups. The RNA viroid generation was catalysed by actinides. The RNA viroids can bind with proteins having prion like domains forming ribonucleoproteins. These ribonucleoproteins can give an abnormal conformation to the protein resulting in generation of abnormal prions. The abnormal prions can act as a

template to convert normal proteins with normal configuration to abnormal conformation. This can result in amyloidogenesis. The abnormal configured proteins will resist lysosomal digestion and accumulate as amyloid. The results are expressed in tables 1-2 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1 *Effect of cerium and antibiotics on cytochrome F420.*

Group	CYT F420 % (Increase with Cerium)		CYT F420 % (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**
Normal	4.48	0.15	18.24	0.66
DM	22.59	1.86	57.05	8.45
CVA	22.29	1.66	59.02	7.50
CAD	22.06	1.61	57.81	6.04
	F value 306.749 P value < 0.001		F value 130.054 P value < 0.001	

Table 2 *Effect of cerium and antibiotics on free RNA.*

Group	RNA % change (Increase with Cerium)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**
Normal	4.37	0.13	18.38	0.48
DM	23.33	1.86	66.46	3.65
CVA	23.32	1.74	65.67	4.16
CAD	23.11	1.52	66.68	3.97
	F value 427.828 P value < 0.001		F value 654.453 P value < 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source. The archaeal origin of the self replicating RNA was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an

alternate actinide based enzymes or metalloenzymes in the system as indicated by cerium induced increase in enzyme activities. There was an increase in free RNA indicating self replicating RNA viroids. The actinides modulate RNA folding and catalyse its ribozymal action. Digoxin can cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities. The RNA viroids can bind with proteins having prion like domains forming ribonucleoproteins. These ribonucleoproteins can give an abnormal conformation to the protein resulting in generation of abnormal prions. The abnormal prions can act as a template to convert normal proteins with normal configuration to abnormal conformation. This can result in amyloidogenesis. The abnormal configured proteins will resist lysosomal digestion and accumulate as amyloid. Amyloidogenesis has been implicated in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The islet cell associated amyloid in diabetes mellitus is a prion protein. Prion diseases are conformational diseases.

The RNA viroids generated from actinidic archaea can bind to proteins with prion like domains resulting in generation of ribonucleoproteins. Ribonucleoproteins with abnormal conformation can act as a template for normal proteins with prion like domains to change to abnormal conformation. This results in generation of prion proteins with abnormal conformation resisting lysosomal digestion and generating amyloid. These systemic diseases are due to actinidic archaeal generated RNA viroid induced prion protein generation and amyloidogenesis. Prion proteins have been implicated in metabolic syndrome x, CVA and CAD. The islet cell associated amyloid in diabetes mellitus is a prion protein. The present study shows that the same prion protein mechanism can operate in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Actinidic archaeal induced RNA viroids generated prions can be transferred

between individuals indicating the infective nature of metabolic syndrome x, CVA and CAD.

The global warming results in increased growth of actinidic archaea and neanderthalisation of the homo sapien species. The actinidic archaea secreted viroids can generate ribonucleoproteins by binding to proteins with prion like domains. This generates amyloidogenesis and leads to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The widespread incidence of these systemic diseases leads to extinction of the neanderthalised species.

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Neo-Neanderthalisation and Metabolic Syndrome-Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke

Introduction

Actinidic archaea has been related to global warming and human diseases especially metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The growth of endosymbiotic actinidic archaea in relation to climate change and global warming leads to neanderthalisation of the human mind-body system. Neanderthal anthropometry and metabolonomics has been described in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD especially the Warburg phenotype and hyperdigoxinemia. Digoxin produced by archaeal cholesterol catabolism produces Neanderthalisation. Prefrontal cortical atrophy and cerebellar hyperplasia has been related to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD in this communication. This leads on to dysautonomia with sympathetic hyperactivity and parasympathetic neuropathy in these disorders. Actinidic archaeal related cerebellar dominance leads to changes in brain function. The data is described in this paper[1-16].

Materials and Methods

Fifteen cases, each of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD as well as internet addicts were selected for the study. Each case had an age and sex matched control. Neanderthal anthropometric and phenotypic measurements which included protruding supra-orbital ridges, dolichocephalic skull, small mandible, prominent mid face and nose, short upper and lower limbs, prominent trunk, low index finger-ring finger ratio and fair complexion were evaluated in the cases study. Autonomic function tests were done to assess the sympathetic and parasympathetic system in each case. CT scan of the head was done to have a volumetric assessment of the prefrontal cortex and cerebellum.

Blood cytochrome F420 activity was assessed by spectrophotometric measurement.

Results

All the case groups studied had higher percentage of Neanderthal anthropometric and phenotypic measurements. There was low index finger-ring finger ratio suggestive of high testosterone levels in all the patient population studied. In all the case groups studied, there also was prefrontal cortex atrophy and cerebellar hyperplasia. Similarly in the all the case groups studied, there was dysautonomia with sympathetic overactivity and parasympathetic neuropathy. Cytochrome F420 was detected in the entire case group studied showing endosymbiotic archaeal overgrowth.

Table 1 *Neanderthal phenotype and systemic disease.*

Disease	Cyt F420	Neanderthal phenotype	Low index finger-ring finger ratio
Diabetes mellitus	65%	72%	72%
CAD	75%	85%	74%
CVA	80%	75%	75%
Internet users	65%	72%	69%

Table 2 *Neanderthal phenotype and brain dysfunction.*

Disease	Dysautonomia	Prefrontal cortex atrophy	Cerebellar hypertrophy
Diabetes mellitus	64%	84%	69%
CAD	75%	73%	72%
CVA	69%	74%	76%
Internet users	74%	84%	82%

Discussion

Neanderthal metabolonomics contribute to the pathogenesis of these disorders. There were Neanderthal phenotypic features in all the case groups studied as well as low index finger-ring finger ratios suggestive of increased testosterone levels. Neanderthalisation of the mind-body system occurs due to increased growth of actinidic archaea as a consequence of global warming. Neanderthalisation of the mind leads to cerebellar dominance and prefrontal cortex atrophy. This leads to dysautonomia with parasympathetic neuropathy and sympathetic hyperactivity. This can lead to the pathogenesis of type 2 diabetes mellitus with CAD and CVA.

Global warming and the ice age produces increased growth of extremophiles. This leads to increased growth of actinidic archaeal endosymbiosis in humans. There is archaeal proliferation in the gut which enters the cerebellum and brain stem by reverse axonal transport via the vagus. The cerebellum and brain stem can be considered as an archaeal colony. The archaea are cholesterol catabolising and use cholesterol as a carbon and energy source. The actinidic archaea activates the toll receptor HIF alpha inducing the Warburg phenotype resulting in increased glycolysis with generation of glycine as well as pyruvate dehydrogenase suppression. The accumulated pyruvate enters the GABA shunt generating of succinyl CoA and glycine. The archaeal catabolism of cholesterol produces ring oxidation and generation of pyruvate which also enters the GABA shunt scheme producing glycine and succinyl CoA. This leads to increased synthesis of porphyrins. In the setting of digoxin induced sodium potassium ATPase inhibition the dipolar porphyrins produce a pumped phonon system resulting in the Frohlich model Bose-Einstein condensate and quantal perception of low level EMF. Low level EMF pollution is common with internet usage. Perception of low level of EMF leads to neanderthalisation of

the brain with prefrontal cortex atrophy and cerebellar hyperplasia. The archaea which reaches the cerebellum from the gut via the vagus nerve proliferates and makes the cerebellum dominant with resultant suppression and atrophy of the prefrontal cortex. This leads to wide spread autistic and schizophrenic traits in population. The actinidic archaea induces the Warburg phenotype with increased glycolysis, PDH inhibition and mitochondrial suppression. This produces neanderthalisation of the mind-body system. This leads to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The actinidic archaea secretes RNA viroids which block HERV expression by RNA interference. The HERV suppression contributes to the inhibition of prefrontal cortex development in Neanderthals and cerebellar dominance. Archaeal digoxin produces sodium potassium ATPase inhibition and magnesium depletion causing reverse transcriptase inhibition and decreased generation of HERV. The HERV contributes to the dynamicity of the genome and are required for the development of the prefrontal cortex. The HERV suppression contributes to retroviral resistance in Neanderthals. The actinidic archaea catabolises cholesterol leading to cholesterol depleted state. Cholesterol depletion also leads to poor synaptic connectivity and decreased development of prefrontal cortex. This is not genetic change but a form of symbiotic change with endosymbiotic actinidic archaeal growth in the body and brain. This brain change leads to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

Internet use and low level EMF pollution is common in this century. This results in increased low level EMF perception by the brain by the digoxin-porphyrin mediated pumped phonon system created Bose-Einstein condensates contributing to prefrontal cortex atrophy and cerebellar dominance. Cerebellar dominance leads to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The porphyrin mediates extrasensory perception of low level EMF. This

can also contributes to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD in Neanderthals.

The modern population is a hybrid of homo sapiens and homo neanderthalis. The extrasensory/quantal perception due to dipolar porphyrins and digoxin induced sodium potassium ATPase inhibition and the generated pumped phonon system mediated quantal perception of low level EMF. This leads to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The archaeal cholesterol catabolism leads to increased synthesis of digoxin which can modulate glucose transport into the cell and insulin sensitivity. Digoxin promotes tryptophan transport over tyrosine. Tyrosine deficiency leads to dopamine deficiency and morphine deficiency. This leads to a morphine deficiency syndrome in Neanderthals. This contributes to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. This can also contribute to addiction and eating behaviour in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

The Neanderthals were essentially meat eaters taking a ketogenic diet. The acetoacetic acid is converted to acetyl CoA which enters the TCA cycle. When the Neanderthal hybrids consume a glucogenic diet owing to the spread of settled civilisation it produces pyruvate accumulation owing to PDH suppression in Neanderthals. The increased archaeal growth activates the toll receptor and induces HIF alpha resulting in increased glycolysis, PDH suppression and mitochondrial dysfunction-the Warburg phenotype. The pyruvate enters the GABA shunt pathway producing glutamate, ammonia and porphyrins resulting in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Neanderthals consuming a ketogenic diet produces more of GABA an inhibitory neurotransmitter. There is less production of glutamate the predominant excitatory neurotransmitter of the prefrontal cortex and consciousness pathways. This leads onto dominance of cerebellar function. The Neanderthal

hybrids have cerebellar dominance and less of conscious behaviour. The predominant homo sapiens had prefrontal cortex dominance over the cerebellum resulting in more of conscious behaviour. This leads to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

The Neanderthals consuming a glucogenic diet produces increased glycolysis in the setting of PDH inhibition. This produces the Warburg phenotype. The predominance of glycolysis and suppression of mitochondrial function results in glycemia and metabolic syndrome-type 2 diabetes mellitus with CAD and CVA. The increased mitochondrial PT pore hexokinase leads to mitochondrial dysfunction resulting in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The glycolytic intermediate 3-phosphoglycerate is converted to glycine resulting in NMDA excitotoxicity and metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

The cerebellar hyperplasia results in sympathetic hyperactivity and parasympathetic neuropathy. Vagal neuropathy and sympathetic over activity can contribute to glycogenolysis and lipolysis resulting in metabolic syndrome x. Vagal neuropathy and sympathetic over activity can contribute to metabolic syndrome x, CVA and CAD. Cerebellar dominance and cerebellar cognitive affective dysfunction can contribute to metabolic syndrome x, CVA and CAD. The increased porphyrin synthesis resulting from succinyl CoA generated by GABA shunt and glycine generated by glycolysis contributes to increased extrasensory perception of low level EMF important in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

The archaeal cholesterol catabolism generates digoxin which produces sodium potassium ATPase inhibition and increase in intracellular calcium and decrease in intracellular magnesium. The increase in intracellular calcium opens the mitochondrial PT pore resulting in mitochondrial dysfunction and metabolic

syndrome-type 2 diabetes mellitus, CVA and CAD. The increase in intracellular calcium can modulate the neurotransmitter release from presynaptic vesicles. This can modulate neurotransmission. Digoxin induced magnesium depletion can remove the magnesium block on the NMDA receptor resulting in NMDA excitotoxicity. Digoxin induced magnesium depletion can inhibit reverse transcriptase activity and HERV generation modulating the dynamicity of the genome. Digoxin induced intracellular calcium accumulation and magnesium depletion can modulate G-protein and protein tyrosine kinase dependent neurotransmitter and endocrine receptors. This can produce digoxin induced neuro-immuno-endocrine integration. Digoxin functions as a neanderthal master hormone. This leads to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

The actinidic archaea are cholesterol catabolising and leads to low levels of testosterone and estrogen. The Neanderthals consume a low fibre diet with low lignan content. The actinidic archaea has cholesterol catabolising enzymes generating more of testosterone than estrogens. This contributes to estrogen deficiency and testosterone overactivity. The Neanderthal population is hypermales with concomitant right hemispheric dominance and cerebellar dominance. Testosterone suppresses left hemispheric function. The high testosterone levels in Neanderthals contribute to a bigger brain. The Neanderthals males as well as females had a higher level of testosterone contributing to gender equality and gender neutral states. There was group identity and group motherhood with no differences between roles of both males and females. This also resulted in matrilinearity. The higher testosterone levels in males as well as females led to alternate type of sexuality and aberrant behaviour. The homo sapiens eat a high fibre diet with low cholesterol and high lignan content contributing to estrogen dominance, left hemispheric dominance and cerebellar hypoplasia. Homo sapiens had higher reproductive rates and overtook the

Neanderthal population resulting in its extinction. This leads to a higher incidence of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The homo sapien population was conservative with normal sexual mores, family values and patriarchal type of behaviour. The role of females the homo sapien community was inferior to males. The increasing generation of Neanderthal hybrids due to climate change mediated archaeal overgrowth leads to gender equality and equidominance of male and female in this century and higher incidence of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

The cholesterol catabolism results in cholesterol depletion and bile acid deficiency. Bile acids bind to FXR, LXR and PXR modulating lipid and carbohydrate metabolism. This leads to metabolic syndrome-type 2 diabetes mellitus in the presence of bile acid deficiency. Bile acid uncouples oxidative phosphorylation and its deficiency leads to obesity of metabolic syndrome x. Cholesterol depletion also leads to vitamin D deficiency. Vitamin D binds to VDR and produces immunomodulation. Vitamin D deficiency can also produce rickets and contribute to the phenotypic features of Neanderthals. Vitamin D deficiency can contribute to brain development resulting in macrocephaly. Vitamin D deficiency contributes to insulin resistance and truncal obesity of Neanderthals. Vitamin D deficiency contributes to the fairness of the Neanderthal skin as a phenotypic adaptation. The Neanderthal phenotypic features are due to vitamin D deficiency and insulin resistance.

Thus global warming and increased endosymbiotic actinidic archaeal growth leads to cholesterol catabolism and generation of the Warburg phenotype resulting in increased porphyrin synthesis, extrasensory low EMF perception, prefrontal cortex atrophy, insulin resistance and cerebellar dominance. This leads on to neanderthalisation of the body and brain and higher incidence of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

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A Neo-Neanderthalisation Related Porphyrin Metabolic Dysfunction Underlies the Metabolic Syndrome-Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke

Introduction

Actinidic archaea is described as an endosymbiont in humans and can induce porphyrinuria in humans. The study aims to relate actinidic archaea to the pathogenesis of essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described. Increased actinidic archaeal growth leads to neanderthalisation of homo sapiens and generation of Neanderthal metabolonomics. Neanderthal metabolonomics results in porphyria. Actinidic archaea have a mevalonate pathway and are cholesterol catabolising. They can use cholesterol as a carbon and energy source. Archaeal cholesterol catabolism can generate porphyrins via the cholesterol ring oxidase generated pyruvate and GABA shunt pathway. Archaea can produce a secondary porphyria by inducing the enzyme heme oxygenase resulting in heme depletion and activation of the enzyme ALA synthase. The study also aims to relate porphyrins to the pathogenesis of essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. This syndrome complex with porphyrinuria can exist as isolated entities or in differing combinations. It constitutes an acquired porphyrin metabolic defect resulting from growth of endosymbiontic actinidic archaea as well as due to environmental pollution. Environmental pollution with pesticides and toxins induces cytochrome P450 enzyme resulting in heme deficiency, ALA synthase induction and porphyrin synthesis. This can be considered as a disorder of civilisational progress. The role of archaeal porphyrins in regulation of cell functions and neuro-immuno-endocrine integration is discussed. A porphyrin metabolic dysfunction related essential hypertension with cardiac autonomic

neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease is described[1-5]. Neo-neanderthalisation porphyric syndrome underlies this disorder-metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

Materials and Methods

The following groups were included in the study: essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. There were also 10 normal people with right hemispheric dominance, left hemispheric dominance and bi-hemispheric dominance drawn from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420, free RNA, free DNA, polycyclic aromatic hydrocarbon, hydrogen peroxide, pyruvate, ammonia, glutamate, delta aminolevulinic acid, succinate, glycine and digoxin. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Polycyclic aromatic hydrocarbon was estimated by measuring hydrogen peroxide liberated by using glucose reagent. The study also involved estimating the following parameters in the patient population-digoxin, bile acid, hexokinase, porphyrins, pyruvate, glutamate, ammonia, acetyl CoA, acetyl

choline, HMG CoA reductase, cytochrome C, blood ATP, ATP synthase, ERV RNA (endogenous retroviral RNA), H_2O_2 (hydrogen peroxide), NOX (NADPH oxidase), TNF alpha and heme oxygenase[6-9]. Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in section 1-tables 1-6 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time. There was upregulated archaeal porphyrin synthesis in the patient population which was archaeal in origin as indicated by actinide catalysis of the reactions. The cholesterol oxidase pathway generated pyruvate which entered the GABA shunt pathway. This resulted in synthesis of succinate and glycine which are substrates for ALA synthase.

The study showed the patient's blood and right hemispheric dominance had increased heme oxygenase activity and porphyrins. The hexokinase activity was high. The pyruvate, glutamate and ammonia levels were elevated indicating blockade of PDH activity, and operation of the GABA shunt pathway. The acetyl CoA levels were low and acetyl choline was decreased. The cyto C levels

were increased in the serum indicating mitochondrial dysfunction suggested by low blood ATP levels. This was indicative of the Warburg's phenotype. There were increased NOX and TNF alpha levels indicating immune activation. The HMG CoA reductase activity was high indicating cholesterol synthesis. The bile acid levels were low indicating depletion of cytochrome P450. The normal population with right hemispheric dominance had values resembling the patient population with increased porphyrin synthesis. The normal population with left hemispheric dominance had low values with decreased porphyrin synthesis.

Section 1: Experimental Study

Table 1 *Effect of rutile and antibiotics on cytochrome F420 and PAH.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66	4.45	0.14	18.25	0.72
HBP	23.12	2.00	56.90	6.94	23.26	1.53	60.91	7.59
CAD/CVA	22.06	1.61	57.81	6.04	23.46	1.91	61.56	4.61
Endo failure	21.68	1.90	57.93	9.64	22.61	1.42	64.48	6.90
	F value 306.749 P value < 0.001		F value 130.054 P value < 0.001		F value 391.318 P value < 0.001		F value 257.996 P value < 0.001	

Table 2 *Effect of rutile and antibiotics on free RNA and DNA.*

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy+Cipro)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
HBP	23.52	1.65	64.15	4.60	23.29	1.92	65.39	3.95
CAD/CVA	23.30	1.42	65.07	4.95	23.11	1.52	66.68	3.97
Endo failure	22.12	2.44	63.69	5.14	23.33	1.35	66.83	3.27
	F value 337.577 P value < 0.001		F value 356.621 P value < 0.001		F value 427.828 P value < 0.001		F value 654.453 P value < 0.001	

Table 3 *Effect of rutile and antibiotics on digoxin and delta aminolevulinic acid.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		ALA % (Increase with Rutile)		ALA % (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	0.11	0.00	0.054	0.003	4.40	0.10	18.48	0.39
HBP	0.55	0.03	0.192	0.040	23.67	1.68	66.50	3.58
CAD/CVA	0.53	0.06	0.212	0.045	23.17	1.88	68.53	2.65
Endo failure	0.53	0.08	0.205	0.041	23.20	1.57	66.65	4.26
	F value 135.116 P value < 0.001		F value 71.706 P value < 0.001		F value 372.716 P value < 0.001		F value 556.411 P value < 0.001	

Table 4 *Effect of rutile and antibiotics on succinate and glycine.*

Group	Succinate % (Increase with Rutile)		Succinate % (Decrease with Doxy+Cipro)		Glycine % change (Increase with Rutile)		Glycine % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.41	0.15	18.63	0.12	4.34	0.15	18.24	0.37
HBP	23.81	1.90	66.95	3.67	23.12	1.71	65.12	5.58
CAD/CVA	22.92	2.14	67.54	3.65	21.93	2.29	63.70	5.63
Endo failure	21.88	1.19	66.28	3.60	23.02	1.65	67.61	2.77
	F value 403.394 P value < 0.001		F value 680.284 P value < 0.001		F value 348.867 P value < 0.001		F value 364.999 P value < 0.001	

Table 5 *Effect of rutile and antibiotics on pyruvate and glutamate.*

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy+Cipro)		Glutamate (Increase with Rutile)		Glutamate (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.34	0.21	18.43	0.82	4.21	0.16	18.56	0.76
HBP	22.63	0.88	56.40	8.59	22.96	2.12	65.11	5.91
CAD/CVA	21.07	1.79	63.90	7.13	22.47	2.17	65.97	4.62
Endo failure	21.91	1.71	58.45	6.66	22.88	1.87	65.45	5.08
	F value 321.255 P value < 0.001		F value 115.242 P value < 0.001		F value 292.065 P value < 0.001		F value 317.966 P value < 0.001	

Table 6 *Effect of rutile and antibiotics on hydrogen peroxide and ammonia.*

Group	H_2O_2 % (Increase with Rutile)		H_2O_2 % (Decrease with Doxy+Cipro)		Ammonia % (Increase with Rutile)		Ammonia % (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.43	0.19	18.13	0.63	4.40	0.10	18.48	0.39
HBP	22.65	2.48	60.19	6.98	23.67	1.68	66.50	3.58
CAD/CVA	22.86	1.91	63.66	6.88	23.17	1.88	68.53	2.65
Endo failure	23.52	1.49	63.24	7.36	23.20	1.57	66.65	4.26
	F value 380.721 P value < 0.001		F value 171.228 P value < 0.001		F value 372.716 P value < 0.001		F value 556.411 P value < 0.001	

Abbreviations

HBP: Hypertension

CAD: Microangiopathic coronary artery disease

CVA: Microangiopathic cerebrovascular disease

Section 2: Patient Study

Table 1

Group	RBC Digoxin (ng/ml RBC Susp)		Cytochrome F 420		HERV RNA (ug/ml)		H_2O_2 (umol/ml RBC)		NOX (OD diff/hr/mgpro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	0.58	0.07	1.00	0.00	17.75	0.72	177.43	6.71	0.012	0.001
RHCD	1.41	0.23	4.00	0.00	55.17	5.85	278.29	7.74	0.036	0.008
LHCD	0.18	0.05	0.00	0.00	8.70	0.90	111.63	5.40	0.007	0.001
Hypertension/ CAN	1.34	0.31	4.00	0.00	51.16	7.78	295.37	3.78	0.035	0.011
CAD	1.22	0.16	4.00	0.00	50.00	5.91	280.89	13.79	0.038	0.009
CVA	1.33	0.27	4.00	0.00	51.06	4.83	287.33	9.47	0.037	0.007
Polyendocrine failure	1.31	0.24	4.00	0.00	50.15	6.96	278.58	12.72	0.039	0.010
F value	60.288		0.001		194.418		713.569		44.896	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Table 2

Group	TNF ALP (pg/ml)		ALA (umol24)		PBG (umol24)		Uroporphyrin (nmol24)		Coproporphyrin (nmol/24)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	17.94	0.59	15.44	0.50	20.82	1.19	50.18	3.54	137.94	4.75
RHCD	78.63	5.08	63.50	6.95	42.20	8.50	250.28	23.43	389.01	54.11
LHCD	9.29	0.81	3.86	0.26	12.11	1.34	9.51	1.19	64.33	13.09
Hypertension/ CAN	82.13	3.97	67.30	5.98	47.25	4.19	286.84	24.18	432.22	50.11
CAD	78.15	3.72	66.66	7.77	47.00	3.81	314.01	17.82	426.14	24.28
CVA	77.59	5.24	69.02	4.86	46.33	4.01	320.85	24.73	402.16	33.80
Polyendocrine failure	79.17	5.88	67.78	4.41	48.03	3.64	306.61	22.47	429.72	24.97
F value	427.654		295.467		183.296		160.533		279.759	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Table 3

Group	Protoporphyrin (Ab unit)		Heme (uM)		Bilirubin (mg/dl)		Biliverdin (Ab unit)		ATP synthase (umol/gHb)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	10.35	0.38	30.27	0.81	0.55	0.02	0.030	0.001	0.36	0.13
RHCD	42.46	6.36	12.47	2.82	1.70	0.20	0.067	0.011	2.73	0.94
LHCD	2.64	0.42	50.55	1.07	0.21	0.00	0.017	0.001	0.09	0.01
Hypertension/ CAN	49.36	4.18	11.81	0.80	1.83	0.09	0.071	0.014	3.34	0.84
CAD	49.51	2.27	11.39	1.10	1.75	0.12	0.080	0.007	2.99	0.65
CVA	46.74	4.28	11.26	0.95	1.82	0.10	0.079	0.009	2.98	0.78
Polyendocrine failure	49.32	5.13	11.60	1.23	1.79	0.08	0.072	0.013	3.29	0.63
F value	424.198		1472.05		370.517		59.963		54.754	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Table 4

Group	SE ATP (umol/dl)		Cyto C (ng/ml)		Lactate (mg/dl)		Pyruvate (umol/l)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	0.42	0.11	2.79	0.28	7.38	0.31	40.51	1.42
RHCD	2.24	0.44	12.39	1.23	25.99	8.10	100.51	12.32
LHCD	0.02	0.01	1.21	0.38	2.75	0.41	23.79	2.51
Hypertension/CAN	1.27	0.26	12.65	1.06	24.28	1.69	95.44	12.04
CAD	1.57	0.37	11.51	0.47	22.83	0.82	97.29	12.45
CVA	1.49	0.27	12.74	0.80	23.03	1.26	103.25	9.49
Polyendocrine failure	1.59	0.38	12.29	0.89	24.87	4.14	95.55	7.20
F value	67.588		445.772		162.945		154.701	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 5

Group	RBC Hexokinase (ug glu phos/ hr/mgpro)		ACOA (mg/dl)		ACH (ug/ml)		Glutamate (mg/dl)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	1.66	0.45	8.75	0.38	75.11	2.96	0.65	0.03
RHCD	5.46	2.83	2.51	0.36	38.57	7.03	3.19	0.32
LHCD	0.68	0.23	16.49	0.89	91.98	2.89	0.16	0.02
Hypertension/CAN	9.30	3.98	1.95	0.06	35.02	5.85	3.14	0.32
CAD	8.88	3.09	2.37	0.44	49.19	6.86	3.61	0.28
CVA	7.87	2.72	2.25	0.44	37.45	7.93	3.31	0.43
Polyendocrine failure	9.84	2.43	2.11	0.19	38.40	7.74	3.45	0.49
F value	18.187		1871.04		116.901		200.702	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 6

Group	Se. ammonia (ug/dl)		HMG Co A (HMG CoA/MEV)		Bile Acid (mg/ml)	
	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	50.60	1.42	1.70	0.07	79.99	3.36
RHCD	93.43	4.85	1.16	0.10	25.68	7.04
LHCD	23.92	3.38	2.21	0.39	140.40	10.32
Hypertension/CAN	94.60	8.52	1.08	0.13	28.93	4.93
CAD	93.93	4.86	1.07	0.12	24.55	6.26
CVA	103.18	27.27	1.05	0.09	22.39	3.35
Polyendocrine failure	92.47	3.97	1.08	0.11	23.28	5.81
F value	61.645		159.963		635.306	
P value	< 0.001		< 0.001		< 0.001	

Abbreviations

BHCD: Bi-hemispheric chemical dominance

RHCD: Right hemispheric chemical dominance

LHCD: Left hemispheric chemical dominance

CAN: Coronary autonomic neuropathy

CAD: Microangiopathic coronary artery disease

CVA: Microangiopathic cerebrovascular disease

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[2, 10]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an

alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[11]. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis[12]. The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide[10]. The pyruvate gets converted to glutamate and ammonia by the GABA shunt pathway. The pyruvate is converted to glutamate by serum glutamate pyruvate transaminase. The glutamate gets acted upon by glutamate dehydrogenase to generate alpha ketoglutarate and ammonia. Alanine is most commonly produced by the reductive amination of pyruvate via alanine transaminase. This reversible reaction involves the interconversion of alanine and pyruvate, coupled to the interconversion of alpha-ketoglutarate (2-oxoglutarate) and glutamate. Alanine can contribute to glycine. Glutamate is acted upon by Glutamic acid decarboxylase to generate GABA. GABA is converted to succinic semialdehyde by GABA transaminase. Succinic semialdehyde is converted to succinic acid by succinic semialdehyde dehydrogenase. Glycine combines with succinyl CoA to generate delta aminolevulinic acid catalysed by the enzyme ALA synthase. There was upregulated archaeal porphyrin synthesis in the patient population which was archaeal in origin as indicated by actinide catalysis of the reactions. The cholesterol oxidase pathway generated pyruvate which entered the GABA shunt pathway. This resulted in synthesis of succinate and glycine which are substrates for ALA synthase. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[13]. This can contribute to the pathogenesis of type 2 diabetes mellitus with CAD and CVA.

The porphyrins can contribute to the pathogenesis of essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. The porphyrins can undergo photo-oxidation and autooxidation generating free radicals. The archaeal porphyrins can produce free

radical injury. The porphyrin photo-oxidation generated free radicals which can modulate enzyme function. Redox stress modulated enzymes include pyruvate dehydrogenase, nitric oxide synthase, cystathione beta synthase and heme oxygenase. Free radicals can modulate mitochondrial PT pore function. Free radicals can modulate cell membrane function and inhibit sodium potassium ATPase activity. Free radicals produce NFKB activation, open the mitochondrial PT pore resulting in cell death, produce oncogene activation, activate NMDA receptor and GAD enzyme regulating neurotransmission and generates the Warburg phenotypes activating glycolysis and inhibiting TCA cycle/oxphos. Redox stress induced by porphyrin autooxidation is crucial to the pathogenesis of these functional disorders. The porphyrins can complex and intercalate with the cell membrane producing sodium potassium ATPase inhibition adding on to digoxin mediated inhibition. Porphyrin induced sodium potassium ATPase inhibition can increase the intracellular calcium load as well as produce intracellular magnesium depletion which are crucial to the pathogenesis of these functional disorders. Increased calcium load and magnesium depletion in the cell produce vasospasm, immune activation and mitochondrial dysfunction. Porphyrins can complex with proteins and nucleic acid producing biophoton emission. Porphyrins complexing with proteins can modulate protein structure and function. Porphyrins complexing with DNA and RNA can modulate transcription and translation. Porphyrin modulating protein, DNA and RNA function can contribute to the pathogenesis of these functional disorders. The porphyrin especially protoporphyrins can bind to peripheral benzodiazepine receptors in the mitochondria and modulate its function, mitochondrial cholesterol transport and steroidogenesis. Defective mitochondrial steroidogenesis can contribute to endocrine failure. Peripheral benzodiazepine receptor modulation by protoporphyrins can regulate cell death, cell proliferation, immunity and neural functions. The protoporphyrin modulation of the peripheral benzodiazepine

receptors is important in the pathogenesis of these functional disorders[3-5]. There was an increase in free RNA indicating self replicating RNA viroids and free DNA indicating generation of viroid complementary DNA strands by archaeal reverse transcriptase activity. The actinides and porphyrins modulate RNA folding and catalyse its ribozymal action. Digoxin can cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities. Archaeal pyruvate producing histone deacetylase inhibition and porphyrins intercalating with DNA can produce endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the RNA viroidal complementary DNA into the noncoding region of eukaryotic non coding DNA using HERV integrase as has been described for borna and ebola viruses. The archaea and viroids can also induce cellular porphyrin synthesis. Bacterial and viral infections can precipitate porphyria. Thus porphyrins can regulate genomic function. The viroids and HERV RNA can modulate mRNA function by RNA interference. The viroids and HERV RNA can contribute to the pathogenesis of essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. Thus the porphyrins are key regulatory molecules modulating all aspects of cell function[14, 15]. This can contribute to the pathogenesis of type 2 diabetes mellitus with CAD and CVA.

The possibility of Warburg phenotype induced by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism contributing the pathogenesis of essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease is important. The Warburg phenotype results in inhibition of pyruvate dehydrogenase and the TCA cycle. The pyruvate enters the GABA shunt pathway where it is converted to succinyl CoA. The glycolytic pathway is

upregulated and the glycolytic metabolite phosphoglycerate is converted to serine and glycine. Glycine and succinyl CoA are the substrates for ALA synthesis. The archaea induces the enzyme heme oxygenase. Heme oxygenase converts heme to bilirubin and biliverdin. This depletes heme from the system and results in upregulation of ALA synthase activity resulting in porphyria. Heme inhibits HIF alpha. The heme depletion results in upregulation of HIF alpha activity and further strengthening of the Warburg phenotype. The porphyrin self oxidation results in redox stress which activates HIF alpha and generates the Warburg phenotype. The Warburg phenotype results in channeling acetyl CoA for cholesterol synthesis as the TCA cycle and mitochondrial oxidative phosphorylation are blocked. The archaea uses cholesterol as an energy substrate. Porphyrin and ALA inhibits sodium potassium ATPase. This increases cholesterol synthesis by acting upon intracellular SREBP. The cholesterol is metabolized to pyruvate and then the GABA shunt pathway for ultimate use in porphyrin synthesis. The porphyrins can self organize and self replicate into macromolecular arrays. The porphyrin arrays behave like an autonomous organism and can have intramolecular electron transport generating ATP. The porphyrin macroarrays can store information and can have quantal perception. The porphyrin macroarrays serves the purpose of archaeal energetics and sensory perception. The Warburg phenotype is associated with essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. The increased generation of fructose 1, 6 diphosphate and its channelling to the pentose phosphate pathway generates NADPH activating NOX. NOX activation generates H_2O_2 induced redox stress contributing to induction of NFKB and immune activation. The lymphocytes depend exclusively on glycolysis for its energy needs. The upregulation of glycolysis produces immune activation. Immune activation and cytokine injury can

contribute to the pathogenesis of these functional disorders. NOX induced redox stress mediated by H_2O_2 can contribute to the pathogenesis of these functional disorders. Warburg phenotype associated mitochondrial dysfunction is crucial to the pathogenesis essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease.

The role of archaeal porphyrins in regulation of cell functions and neuro-immuno-endocrine integration is discussed. Protoporphyrine binds to the peripheral benzodiazepine receptor regulating steroid and digoxin synthesis. Increased porphyrin metabolites can contribute to hyperdigoxinemia. Digoxin can modulate the neuro-immuno-endocrine system. Digoxin can produce membrane sodium potassium ATPase inhibition increasing intracellular calcium and reducing intracellular magnesium. Porphyrins can combine with membranes modulating membrane function and producing sodium potassium ATPase inhibition. Digoxin induced intracellular calcium load can activate NFKB producing cytokine injury as well as produce mitochondrial dysfunction. Digoxin induced increased intracellular calcium can produce vasospasm and bronchospasm. Digoxin induced mitochondrial dysfunction can produce redox stress. Hyperdigoxinemia is related to the pathogenesis of essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. These groups of functional disorders can be classified as intracellular calcium overload and magnesium depleted states.

Porphyrins can combine with proteins oxidizing their tyrosine, tryptophan, cysteine and histidine residues producing crosslinking and altering protein conformation and function. This can produce a protein processing dysfunction and defectively processed proteins accumulate in the cell. Porphyrin induced protein processing dysfunction and defective protein function can contribute to essential hypertension with cardiac autonomic neuropathy, polyendocrine

failure and microangiopathic cerebral/coronary disease. Porphyrins can complex with DNA and RNA modulating their function. Porphyrin interpolating with DNA can alter transcription and generate HERV expression. HERV RNA can produce mRNA interference affecting its function. HERV expression can also contribute to the pathogenesis of these functional disorders.

Heme deficiency can also result in disease states. Heme deficiency results in deficiency of heme enzymes. There is deficiency of cytochrome C oxidase and mitochondrial dysfunction. Mitochondrial dysfunction induced energy depletion and redox stress is crucial to the pathogenesis of these functional disorders. Mitochondrial dysfunction induced muscle weakness is crucial in chronic fatigue syndrome. The glutathione peroxidase is dysfunctional and the glutathione system of free radical scavenging does not function. Redox stress is crucial to the pathogenesis of these functional disorders. The cytochrome P450 enzymes involved in steroid and bile acid synthesis have reduced activity leading to steroid-cortisol, activated vitamin D and sex hormones as well as bile acid deficiency states. Heme deficiency also results in defective thyroid peroxidase function and thyroid hormone deficiency. Deficiency of cortisol, thyroid and sex hormones produce the syndrome of endocrine failure. Bile acid deficiency and activated vitamin D deficiency are important in the evolution of these disorders. Activated vitamin D and bile acid like lithocholic acid bind to VDR modulating the immune system. Activated vitamin D deficiency as well as bile acid deficiency can lead to immune activation and cytokine injury important in the pathogenesis of these functional disorders. The heme deficiency results in dysfunction of nitric oxide synthase, heme oxygenase and cystathione beta synthase resulting in lack of gasotransmitters regulating the vascular system and NMDA receptor – NO, CO and H_2S. Heme has got cytoprotective, neuroprotective, anti-inflammatory and antiproliferative effects. Deficiency of NO, CO and H_2S which are vasodilatory gasotransmitters can

contribute to hypertension and cardiac autonomic neuropathy. Sexual dysautonomia combined with gonadal failure can contribute to infertility and asexuality. Heme is also involved in the stress response. Deficient heme induced stress response can lead to panic attacks. Heme deficiency leads to essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease[3-5].

Porphyrins can lead on to an immune activated state. The porphyrin photo-oxidation can generate free radicals which can activate NFKB. This can produce immune activation and cytokine mediated injury. The protoporphyrins binding to mitochondrial benzodiazepine receptors can modulate immune function. Porphyrins can combine with proteins oxidizing their tyrosine, tryptophan, cysteine and histidine residues producing crosslinking and altering protein conformation and function. Porphyrins can complex with DNA and RNA modulating their structure. Porphyrin complexed with proteins and nucleic acids are antigenic and can lead onto autoimmune disease[3, 4]. Immune activation and autoimmunity is crucial to essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. Porphyrins can lead on to an insulin resistance state. The porphyrin photo-oxidation mediated free radical injury can lead to insulin resistance and atherogenesis. Thus archaeal porphyrins can contribute to metabolic syndrome x. Glucose has got a negative effect upon ALA synthase activity. Therefore hyperglycemia may be reactive protective mechanism to increased archaeal porphyrin synthesis. The protoporphyrins binding to mitochondrial benzodiazepine receptors can modulate mitochondrial steroidogenesis and metabolism. Altered porphyrin metabolism has been described in the metabolic syndrome x. Porphyrias can lead onto vascular thrombosis[3, 4]. Insulin resistance states have been related to essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary

disease. The porphyrin photo-oxidation can generate free radicals inducing HIF alpha and producing oncogene activation. The porphyrins can intercalate with DNA producing HERV expression. The HERV particles generated can contribute to the retroviral state. All these functional disorders are associated with the retroviral state. The porphyrins in the blood can combine with bacteria and viruses and the photo-oxidation generated free radicals can kill them. The archaeal porphyrins can modulate bacterial and viral infections. The archaeal porphyrins are regulatory molecules keeping other prokaryotes and viruses on check[3, 4]. Bacterial and viral infections have been related to essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease.

The archaea and viroids can regulate the nervous system including the NMDA/GABA thalamocorticothalamic pathway mediating conscious perception. Porphyrin photo-oxidation can generate free radicals which can modulate NMDA transmission. Free radicals can increase NMDA transmission. Free radicals can induce GAD and increase GABA synthesis. ALA blocks GABA transmission and upregulates NMDA. Protoporphyrins bind to GABA receptor and promote GABA transmission. Thus porphyrins can modulate the thalamocorticothalamic pathway of conscious perception. The dipolar porphyrins, PAH and archaeal magnetite in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated frohlich model superconducting state inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world. ALA can produce sodium potassium ATPase inhibition resulting in a pumped phonon system mediated quantal state involving dipolar porphyrins. Porphyrin molecules have a wave particle existence and can bridge the dividing line between quantal state and particulate state. Thus the porphyrins can mediate conscious and quantal perception.

Porphyrins binding to proteins, nucleic acids and cell membranes can produce biophoton emission. Porphyrins by autooxidation can generate biophotons and are involved in quantal perception. Biophotons can mediate quantal perception. Cellular porphyrins photo-oxidation are involved in sensing of earth magnetic fields and low level biomagnetic fields. Thus prophyrins can mediate extrasensory perception of low level EMF. This can lead to essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. The porphyrins can also modulate hemispheric dominance. There is increased porphyrin synthesis and RHCD and decreased porphyrin synthesis in LHCD. Porphyria can lead to psychiatric disorders and seizures. Right hemispheric chemical dominance is related to essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. All these functional disorders have a neuropsychiatric substratum.

Protoporphyrins block acetyl choline transmission producing a vagal neuropathy with sympathetic overactivity. This can lead to panic syndrome, coronary autonomic neuropathy and hypertension. Vagal neuropathy results in immune activation, vasospasm and vascular disease. A vagal neuropathy underlines metabolic syndrome x and microangiopathic disease. Vagal neuropathy induced immune activation can produce cytokine injury crucial in the pathogenesis of essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. Porphyrin induced increased NMDA transmission and free radical injury can contribute to cell death. Free radicals can produce mitochondrial PT pore dysfunction. This can lead to cytoC leak and activation of the caspase cascade leading to apoptosis and cell death. Porphyrin induced cell death can contribute to the pathogenesis of these disorders. The protoporphyrins binding to mitochondrial benzodiazepine receptors can regulate brain function and cell death[3, 4, 16].

The dipolar porphyrins, PAH and archaeal magnetite in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated Frohlich model superconducting state inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macrosopic world. ALA can produce sodium potassium ATPase inhibition resulting in a pumped phonon system mediated quantal state involving dipolar porphyrins. Porphyrins by autooxidation can generate biophotons and are involved in quantal perception. Biophotons can mediate quantal perception. Cellular porphyrins photo-oxidation are involved in sensing of earth magnetic fields and low level biomagnetic fields. Porphyrins can thus contribute to quantal perception. Low level electromagnetic fields and light can induce porphyrin synthesis. Low level EMF can produce ferrochelatase inhibition as well as heme oxygenase induction contributing to heme depletion, ALA synthase induction and increased porphyrin synthesis. Light also induces ALA synthase and porphyrin synthesis. The increased porphyrin synthesized can contribute to increased quantal perception and can modulate conscious perception. The porphyrin induced biophotons and quantal fields can modulate the source from which low level EMF and photic fields were generated. Thus the porphyrin generated by extraneous low level EMF and photic fields can interact with the source of low level EMF and photic fields modulating it. Thus porphyrins can serve as a bridge between the human brain and the source of low level EMF and photic fields. This serves as a mode of communication between the human brain and EMF storage devices like internet. The porphyrins can also serve as the source of communication with the environment. Environmental EMF and chemicals produce heme oxygenase induction and heme depletion increasing porphyrin synthesis, quantal perception and two-way communication. Thus induction of porphyrin synthesis can serve as a mechanism of communication between

human brain and the environment by extrasensory perception. Low level of EMF exposure can lead to essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. All these functional disorders are increasing in epidemic proportions and environmental pollution with low level of EMF is related to it. These functional disorders are related to civilisational progress.

Porphyrins also have evolutionary significance since porphyria is related to Scythian races and contributes to the behavioural and intellectual characteristics of this group of population. Porphyrins can intercalate into DNA and produce HERV expression. HERV RNA can get converted to DNA by reverse transcriptase which can get integrated into DNA by integrase. This tends to increase the length of the non coding region of the DNA. The increase in non coding region of the DNA is involved in primate and human evolution. Thus, increased rates of porphyrin synthesis would correlate with increase in non coding DNA length. The alteration in the length of the non coding region of the DNA contributes to the dynamic nature of the genome. Thus genetic and acquired porphyrias can lead to alteration in the non coding region of the genome. The alteration of the length of the non coding region of the DNA contributes to the racial and individual differences in populations. An increased length of non coding region as well as increased porphyrin synthesis leads to increased cognitive and creative neuronal function. Porphyrins are involved in quantal perception and regulation of the thalamocorticothalamic pathway of conscious perception. Thus genetic and acquired porphyrias contribute to higher cognitive and creative capacity of certain races. Porphyrias are common among Eurasian Scythian races who have assumed leadership roles in communities and groups. Porphyrins have contributed to human and primate evolution. Scythian races have a higher incidence of essential hypertension with cardiac autonomic

neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. Most of our patient population belonged to this group[3, 4].

An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states-essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease is described. Porphyrin synthesis is crucial in the pathogenesis of these disorders. Porphyrins may serve as regulatory molecules modulating immune, neural, endocrine, metabolic and genetic systems. The porphyrins photo-oxidation generated free radicals can produce immune activation, produce cell death, activate cell proliferation, produce insulin resistance and modulate conscious/quantal perception. The archaeal porphyrins functions as key regulatory molecules with mitochondrial benzodiazepine receptors playing an important role. The porphyrins photo-oxidation generated free radicals can produce immune activation, produce cell death, activate cell proliferation, produce insulin resistance and modulate conscious/quantal perception. Porphyrins can regulate hemispheric dominance. Porphyrins inhibit cholinergic transmission producing a vagal neuropathy and sympathetic overactivity. Heme deficiency can induce the Warburg phenotype contributing to the pathogenesis of essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. Heme deficiency also results in mitochondrial dysfunction as well as dysfunction of the glutathione system of free radicals scavenging. Heme deficiency can affect thyroid peroxidase and cytochrome P450 enzymes involved in steroidal synthesis producing a polyendocrine failure. Heme deficiency can affect the heme enzymes producing the vasodilatory gasotransmitter NO, CO and H_2S synthesis producing hypertension. Porphyrin generated redox stress can induce NFKB producing immune activation. Vagal neuropathy and gasotransmitter deficiency especially of NO can lead to microangiopathic of the coronary and cerebral circulation.

Vagal neuropathy can also contribute to immune activation. Immune activation and vagal neuropathy causes cerebral and coronary microangiopathic disease. Vagal neuropathy with sympathetic overactivity can induce to panic attacks. Protoporhyrin mediated increased digoxin synthesis can contribute to increased intracellular calcium producing essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. The archaeal porphyrins functions as key regulatory molecules with mitochondrial benzodiazepine receptors playing an important role. A porphyrin metabolic defect underlies the pathogenesis of essential hypertension with cardiac autonomic neuropathy, polyendocrine failure and microangiopathic cerebral/coronary disease. This can be called as a civilizational porphyrin metabolic disorder. A neo-neanderthalisation related porphyrin metabolic dysfunction related CVS dyautonomia, coronary/cerebral microangiopathy and polyendocrine failure complex is described. Increased actinidic archaeal growth leads to neanderthalisation of homo sapiens and generation of Neanderthal metabolonomics. Neanderthal metabolonomics results in porphyria. Neo-neanderthalisation porphyric syndrome underlies this disorder.

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Porphyrins and Quantal Perception – Role of Porphyrins in Environmental Communication/Modulation of Digital Information Storage/Processing System – Low Level of Electromagnetic Fields and Metabolic Syndrome-Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke

Introduction

Actinidic archaea has been described as endosymbionts in humans. Actinidic archaea have a mevalonate pathway and are cholesterol catabolising. They can use cholesterol as a carbon and energy source. Archaeal cholesterol catabolism can generate porphyrins via the cholesterol ring oxidase generated pyruvate and GABA shunt pathway. Archaea can produce a secondary porphyria by inducing the enzyme heme oxygenase resulting in heme depletion and activation of the enzyme ALA synthase. The archaea can induce the enzyme heme oxygenase resulting in depletion of heme and induction of ALA synthase. This can lead to porphyrinogenesis. Low level of electromagnetic fields and geomagnetic fields can induce porphyrin synthesis by inhibiting the enzyme ferrochelatase which has got a ferromagnetic core. Inhibition of ferrochelatase produces deficiency of heme resulting in induction of ALA synthase. Low level of EMF can also induce heme oxygenase depleting heme and inducing ALA synthase. Porphyrins can undergo auto-oxidation generating biophotons and a quantal state. Porphyrin auto-oxidation is modulated by low level of electromagnetic fields and geomagnetic fields. Porphyrin microarrays can function as quantal computers storing information and can serve the purpose of extrasensory perception. Porphyrins can serve as a two way communicating bridge between digital information storage systems generating low level electromagnetic fields and human systems. The low level of EMF produced by digital system enhances porphyrin synthesis and serves the purpose of two way extrasensory perception and communication. The porphyrin quantal computers can in turn by biophoton emission modulate digital information storage system. Actinidic archaea have been related to the pathogenesis of metabolic syndrome x, CVA and CAD. An actinide dependent shadow biosphere of archaea and viroids in the above

mentioned disease states is described. Porphyrins have been related to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Porphyrins can mediate the pathogenesis of low level electromagnetic fields inducing the above mentioned disease states. A hypothesis regarding the role of porphyrins and quantal perception as well as the role of porphyrins in environmental communication/modulation of digital information storage/processing system is presented. The relationship between low level of electromagnetic fields and metabolic syndrome-type 2 diabetes mellitus, CAD and CVA is highlighted[1-5].

Materials and Methods

The following groups were included in the study: – metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. There were also 10 normal people with right hemispheric dominance, left hemispheric dominance and bi-hemispheric dominance included in the study selected from the normal population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420, free RNA, free DNA, polycyclic aromatic hydrocarbon, hydrogen peroxide, pyruvate, ammonia, glutamate, delta aminolevulinic acid, succinate, glycine and digoxin. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission

wavelength 520 nm). Polycyclic aromatic hydrocarbon was estimated by measuring hydrogen peroxide liberated by using glucose reagent. The study also involved estimating the following parameters in the patient population-digoxin, bile acid, hexokinase, porphyrins, pyruvate, glutamate, ammonia, acetyl CoA, acetyl choline, HMG CoA reductase, cytochrome C, blood ATP, ATP synthase, ERV RNA (endogenous retroviral RNA), H_2O_2 (hydrogen peroxide), NOX (NADPH oxidase), TNF alpha and heme oxygenase[6-9]. Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients and those with exposure to low level of EMF showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma and those with exposure to low level of EMF caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables section 1: 1-6 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time. There was upregulated archaeal porphyrin synthesis in the patient population and those with exposure to low level of EMF which was archaeal in origin as indicated by actinide catalysis of the reactions. The cholesterol oxidase pathway generated pyruvate which entered the GABA

shunt pathway. This resulted in synthesis of succinate and glycine which are substrates for ALA synthase.

The study showed the patient's blood, those with exposure to low level of EMF and right hemispheric dominance had increased heme oxygenase activity and porphyrins. The hexokinase activity was high. The pyruvate, glutamate and ammonia levels were elevated indicating blockade of PDH activity, and operation of the GABA shunt pathway. The acetyl CoA levels were low and acetyl choline was decreased. The cytoC levels were increased in the serum indicating mitochondrial dysfunction suggested by low blood ATP levels. This was indicative of the Warburg's phenotype. There was increased NOX and TNF alpha level indicating immune activation. The HMG CoA reductase activity was high indicating cholesterol synthesis. The bile acid levels were low indicating depletion of cytochrome P450. The normal population with right hemispheric dominance had values resembling the patient population with increased porphyrin synthesis. The normal population with left hemispheric dominance had low values with decreased porphyrin synthesis.

Section 1: Experimental Study

Table 1 *Effect of rutile and antibiotics on cytochrome F420 and PAH.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66	4.45	0.14	18.25	0.72
DM	22.59	1.86	57.05	8.45	23.40	1.55	65.77	5.27
CVA	22.29	1.66	59.02	7.50	23.23	1.97	65.89	5.05
CAD	22.06	1.61	57.81	6.04	23.46	1.91	61.56	4.61
Low level EMF	22.70	1.87	60.46	8.06	23.73	1.38	65.20	6.20
	F value 306.749 P value < 0.001		F value 130.054 P value < 0.001		F value 391.318 P value < 0.001		F value 257.996 P value < 0.001	

Table 2 *Effect of rutile and antibiotics on free RNA and DNA.*

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy+Cipro)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
DM	23.01	1.67	65.35	3.56	23.33	1.86	66.46	3.65
CVA	22.56	2.46	62.70	4.53	23.32	1.74	65.67	4.16
CAD	23.30	1.42	65.07	4.95	23.11	1.52	66.68	3.97
Low level EMF	22.29	2.05	58.70	7.34	22.29	2.05	67.03	5.97
	F value 337.577 P value < 0.001		F value 356.621 P value < 0.001		F value 427.828 P value < 0.001		F value 654.453 P value < 0.001	

Table 3 *Effect of rutile and antibiotics on digoxin and delta aminolevulinic acid.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		ALA % (Increase with Rutile)		ALA % (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	0.11	0.00	0.054	0.003	4.40	0.10	18.48	0.39
DM	0.47	0.04	0.202	0.025	22.87	1.84	66.31	3.68
CVA	0.56	0.05	0.220	0.052	23.45	1.79	66.32	3.63
CAD	0.53	0.06	0.212	0.045	23.17	1.88	68.53	2.65
Low level EMF	0.51	0.05	0.213	0.033	22.29	2.05	61.91	7.56
	F value 135.116 P value < 0.001		F value 71.706 P value < 0.001		F value 372.716 P value < 0.001		F value 556.411 P value < 0.001	

Table 4 *Effect of rutile and antibiotics on succinate and glycine.*

Group	Succinate % (Increase with Rutile)		Succinate % (Decrease with Doxy+Cipro)		Glycine % change (Increase with Rutile)		Glycine % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.41	0.15	18.63	0.12	4.34	0.15	18.24	0.37
DM	23.70	1.75	68.06	3.52	23.81	1.49	64.89	6.01
CVA	23.66	1.67	65.97	3.36	23.09	1.81	65.86	4.27
CAD	22.92	2.14	67.54	3.65	21.93	2.29	63.70	5.63
Low level EMF	22.29	1.33	65.38	3.62	22.13	2.14	66.26	3.93
	F value 403.394 P value < 0.001		F value 680.284 P value < 0.001		F value 348.867 P value < 0.001		F value 364.999 P value < 0.001	

Table 5 *Effect of rutile and antibiotics on pyruvate and glutamate.*

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy+Cipro)		Glutamate (Increase with Rutile)		Glutamate (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.34	0.21	18.43	0.82	4.21	0.16	18.56	0.76
DM	20.67	1.38	58.75	8.12	23.23	1.88	65.11	5.14
CVA	21.21	2.36	58.73	8.10	21.11	2.25	64.20	5.38
CAD	21.07	1.79	63.90	7.13	22.47	2.17	65.97	4.62
Low level EMF	22.29	2.05	62.37	5.05	21.66	1.94	67.03	5.97
	F value 321.255 P value < 0.001		F value 115.242 P value < 0.001		F value 292.065 P value < 0.001		F value 317.966 P value < 0.001	

Table 6 *Effect of rutile and antibiotics on hydrogen peroxide and ammonia.*

Group	H_2O_2 % (Increase with Rutile)		H_2O_2 % (Decrease with Doxy+Cipro)		Ammonia % (Increase with Rutile)		Ammonia % (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.43	0.19	18.13	0.63	4.40	0.10	18.48	0.39
DM	23.27	1.53	58.91	6.09	22.87	1.84	66.31	3.68
CVA	23.32	1.71	63.15	7.62	23.45	1.79	66.32	3.63
CAD	22.86	1.91	63.66	6.88	23.17	1.88	68.53	2.65
Low level EMF	23.29	1.67	60.52	5.38	22.29	2.05	61.91	7.56
	F value 380.721 P value < 0.001		F value 171.228 P value < 0.001		F value 372.716 P value < 0.001		F value 556.411 P value < 0.001	

Abbreviations

DM: Diabetes mellitus

CVA: Cerebrovascular accident

CAD: Coronary artery disease

Section 2: Patient Study

Table 1

Group	RBC Digoxin (ng/ml RBC Susp)		Cytochrome F 420		HERV RNA (ug/ml)		H_2O_2 (umol/ml RBC)		NOX (OD diff/hr/mgpro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	0.58	0.07	1.00	0.00	17.75	0.72	177.43	6.71	0.012	0.001
RHCD	1.41	0.23	4.00	0.00	55.17	5.85	278.29	7.74	0.036	0.008
LHCD	0.18	0.05	0.00	0.00	8.70	0.90	111.63	5.40	0.007	0.001
DM	1.35	0.26	4.00	0.00	51.98	5.05	280.89	10.58	0.041	0.005
CAD	1.22	0.16	4.00	0.00	50.00	5.91	280.89	13.79	0.038	0.009
CVA	1.33	0.27	4.00	0.00	51.06	4.83	287.33	9.47	0.037	0.007
Exposure to EMF	1.41	0.30	4.00	0.00	51.01	4.77	276.49	10.92	0.038	0.007
F value	60.288		0.001		194.418		713.569		44.896	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Table 2

Group	TNF ALP (pg/ml)		ALA (umol24)		PBG (umol24)		Uroporphyrin (nmol24)		Coproporphyrin (nmol/24)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	17.94	0.59	15.44	0.50	20.82	1.19	50.18	3.54	137.94	4.75
RHCD	78.63	5.08	63.50	6.95	42.20	8.50	250.28	23.43	389.01	54.11
LHCD	9.29	0.81	3.86	0.26	12.11	1.34	9.51	1.19	64.33	13.09
DM	78.36	6.68	64.72	6.81	48.15	3.36	285.46	29.46	422.27	33.86
CAD	78.15	3.72	66.66	7.77	47.00	3.81	314.01	17.82	426.14	24.28
CVA	77.59	5.24	69.02	4.86	46.33	4.01	320.85	24.73	402.16	33.80
Exposure to EMF	76.41	5.96	68.41	5.53	47.27	3.42	288.21	26.17	444.94	38.89
F value	427.654		295.467		183.296		160.533		279.759	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Table 3

Group	Protoporphyrin (Ab unit)		Heme (uM)		Bilirubin (mg/dl)		Biliverdin (Ab unit)		ATP Synthase (umol/gHb)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	10.35	0.38	30.27	0.81	0.55	0.02	0.030	0.001	0.36	0.13
RHCD	42.46	6.36	12.47	2.82	1.70	0.20	0.067	0.011	2.73	0.94
LHCD	2.64	0.42	50.55	1.07	0.21	0.00	0.017	0.001	0.09	0.01
DM	49.80	4.01	12.83	2.07	1.77	0.19	0.067	0.014	3.19	0.89
CAD	49.51	2.27	11.39	1.10	1.75	0.12	0.080	0.007	2.99	0.65
CVA	46.74	4.28	11.26	0.95	1.82	0.10	0.079	0.009	2.98	0.78
Exposure to EMF	50.59	1.71	12.36	1.26	1.75	0.22	0.073	0.013	3.39	1.03
F value	424.198		1472.05		370.517		59.963		54.754	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Table 4

Group	SE ATP (umol/dl)		Cyto C (ng/ml)		Lactate (mg/dl)		Pyruvate (umol/l)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	0.42	0.11	2.79	0.28	7.38	0.31	40.51	1.42
RHCD	2.24	0.44	12.39	1.23	25.99	8.10	100.51	12.32
LHCD	0.02	0.01	1.21	0.38	2.75	0.41	23.79	2.51
DM	1.97	0.11	12.95	0.56	25.56	7.93	96.30	10.33
CAD	1.57	0.37	11.51	0.47	22.83	0.82	97.29	12.45
CVA	1.49	0.27	12.74	0.80	23.03	1.26	103.25	9.49
Exposure to EMF	1.37	0.27	12.26	1.00	23.31	1.46	103.28	11.47
F value	67.588		445.772		162.945		154.701	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 5

Group	RBC hexokinase (ug glu phos/hr/mgpro)		ACOA (mg/dl)		ACH (ug/ml)		Glutamate (mg/dl)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	1.66	0.45	8.75	0.38	75.11	2.96	0.65	0.03
RHCD	5.46	2.83	2.51	0.36	38.57	7.03	3.19	0.32
LHCD	0.68	0.23	16.49	0.89	91.98	2.89	0.16	0.02
DM	7.05	1.86	2.17	0.40	41.31	10.69	3.53	0.44
CAD	8.88	3.09	2.37	0.44	49.19	6.86	3.61	0.28
CVA	7.87	2.72	2.25	0.44	37.45	7.93	3.31	0.43
Exposure to EMF	7.58	3.09	2.14	0.19	37.75	7.31	3.47	0.37
F value	18.187		1871.04		116.901		200.702	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 6

Group	Se. Ammonia (ug/dl)		HMG CoA (HMG CoA/MEV)		Bile acid (mg/ml)	
	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	50.60	1.42	1.70	0.07	79.99	3.36
RHCD	93.43	4.85	1.16	0.10	25.68	7.04
LHCD	23.92	3.38	2.21	0.39	140.40	10.32
DM	93.38	7.76	1.09	0.12	22.77	4.94
CAD	93.93	4.86	1.07	0.12	24.55	6.26
CVA	103.18	27.27	1.05	0.09	22.39	3.35
Exposure to EMF	102.62	26.54	1.00	0.07	22.58	5.07
F value	61.645		159.963		635.306	
P value	< 0.001		< 0.001		< 0.001	

Abbreviations

NO/BHCD: Normal/Bi-hemispheric chemical dominance

RHCD: Right hemispheric chemical dominance

LHCD: Left hemispheric chemical dominance

DM: Diabetes mellitus

CAD: Coronary artery disease

CVA: Cerebrovascular accident

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[2, 10]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an

alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[11]. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis[12]. The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide[10]. The pyruvate gets converted to glutamate and ammonia by the GABA shunt pathway. The pyruvate is converted to glutamate by serum glutamate pyruvate transaminase. The glutamate gets acted upon by glutamate dehydrogenase to generate alpha ketoglutarate and ammonia. Alanine is most commonly produced by the reductive amination of pyruvate via alanine transaminase. This reversible reaction involves the interconversion of alanine and pyruvate, coupled to the interconversion of alpha-ketoglutarate (2-oxoglutarate) and glutamate. Alanine can contribute to glycine. Glutamate is acted upon by Glutamic acid decarboxylase to generate GABA. GABA is converted to succinic semialdehyde by GABA transaminase. Succinic semialdehyde is converted to succinic acid by succinic semialdehyde dehydrogenase. Glycine combines with succinyl CoA to generate delta aminolevlunic acid catalysed by the enzyme ALA synthase. There was upregulated archaeal porphyrin synthesis in the patient population which was archaeal in origin as indicated by actinide catalysis of the reactions. The cholesterol oxidase pathway generated pyruvate which entered the GABA shunt pathway. This resulted in synthesis of succinate and glycine which are substrates for ALA synthase. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[13]. This underlies the basis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

Low level electromagnetic fields and its porphyrin messengers can regulate the brain mediating conscious and quantal perception. Porphyrin microarrays serve the purpose of quantal and conscious perception. The archaea and viroids via porphyrin synthesis can regulate the nervous system including the NMDA/GABA

thalamocorticothalamic pathway mediating conscious perception. Porphyrin photo-oxidation can generate free radicals which can modulate NMDA transmission. Free radicals can increase NMDA transmission. Free radicals can induce GAD and increase GABA synthesis. ALA blocks GABA transmission and upregulates NMDA. Protoporphyrins bind to GABA receptor and promote GABA transmission. Thus porphyrins can modulate the thalamocorticothalamic pathway of conscious perception. The dipolar porphyrins in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated Frohlich model superconducting state inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world. ALA can produce sodium potassium ATPase inhibition resulting in a pumped phonon system mediated quantal state involving dipolar porphyrins. Porphyrin molecules have a wave particle existence and can bridge the dividing line between quantal state and particulate state. Thus the porphyrins can mediate conscious and quantal perception. Porphyrins binding to proteins, nucleic acids and cell membranes can produce biophoton emission. Porphyrins by auto-oxidation can generate biophotons and are involved in quantal perception. Biophotons can mediate quantal perception. Cellular porphyrins photo-oxidation are involved in sensing of earth magnetic fields and low level biomagnetic fields. Thus porphyrin microarrays can function as a quantal computer mediating extrasensory perception. Porphyrin microarrays in human systems and brain owing to the wave particle nature of porphyrins can bridge the quantal world and particulate world. The porphyrins can modulate hemispheric dominance. There is increased porphyrin synthesis and RHCD and decreased porphyrin synthesis in LHCD. The increase in archaeal porphyrins can contribute to the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Porphyria can lead to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Altered porphyrin

metabolism has been described in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Porphyrins by modulating conscious and quantal perception is involved in the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[3, 4, 16]. Thus porphyrins microarrays can function as a quantal brain modulating extrasensory quantal perception. Porphyrin microarrays can function as a quantal brain in communication with digital world and geomagnetic fields.

The dipolar porphyrins in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated Frohlich model superconducting state inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world. ALA can produce sodium potassium ATPase inhibition resulting in a pumped phonon system mediated quantal state involving dipolar porphyrins. Porphyrins by auto-oxidation can generate biophotons and are involved in quantal perception. Biophotons can mediate quantal perception. Porphyrin auto-oxidation is modulated by low level of electromagnetic fields and geomagnetic fields. Cellular porphyrins photo-oxidation are involved in sensing of earth magnetic fields and low level biomagnetic fields. Porphyrins can thus contribute to quantal perception. Low level electromagnetic fields and light can induce porphyrin synthesis. Low level EMF can produce ferrochelatase inhibition as well as heme oxygenase induction contributing to heme depletion, ALA synthase induction and increased porphyrin synthesis. Light also induces ALA synthase and porphyrin synthesis. The increased porphyrin synthesized can contribute to increased quantal perception and can modulate conscious perception. The human porphyrin microarrays induced biophotons and quantal fields can modulate the source from which low level EMF and photic fields were generated. Thus the porphyrin generated by extraneous low level EMF and photic fields can interact with the source of low level EMF and photic fields modulating it. Thus

porphyrins can serve as a bridge between the human brain and the source of low level EMF and photic fields. This serves as a mode of communication between the human brain and digital EMF storage devices like internet. The porphyrins can also serve as the source of communication with the environment. Environmental EMF and chemicals produce heme oxygenase induction and heme depletion increasing porphyrin synthesis, quantal perception and two-way communication. Thus induction of porphyrin synthesis can serve as a mechanism of communication between human brain and the environment by extrasensory perception. Porphyrin microarrays can function as quantal computers storing information and can serve the purpose of extrasensory perception. Porphyrins can serve as a two way communicating bridge between digital information storage systems generating low level electromagnetic fields and human systems. The low level of EMF produced by digital system enhances porphyrin synthesis and serves the purpose of two way extrasensory perception and communication. The human porphyrin quantal computers can in turn by biophoton emission modulate digital information storage system. This perception of low level EMF contributes to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

Low level of electromagnetic fields and its porphyrin messengers can induce the Warburg phenotype. An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described. The archaea can synthesize porphyrins and induce porphyrin synthesis. Porphyrins have been related to metabolic syndrome x, CVA and CAD. Porphyrins can mediate the effect of low level electromagnetic fields inducing the Warburg phenotype leading to the above mentioned disease states. The Warburg phenotype results in inhibition of pyruvate dehydrogenase and the TCA cycle. The pyruvate enters the GABA shunt pathway where it is converted to succinyl CoA. The glycolytic pathway is upregulated and the glycolytic metabolite phosphoglycerate is

converted to serine and glycine. Glycine and succinyl CoA are the substrates for ALA synthesis. The archaea induces the enzyme heme oxygenase. Heme oxygenase converts heme to bilirubin and biliverdin. This depletes heme from the system and results in upregulation of ALA synthase activity resulting in porphyria. Heme inhibits HIF alpha. The heme depletion results in upregulation of HIF alpha activity and further strengthening of the Warburg phenotype. The porphyrin self oxidation results in redox stress which activates HIF alpha and generates the Warburg phenotype. The Warburg phenotype results in channelling acetyl CoA for cholesterol synthesis as the TCA cycle and mitochondrial oxidative phosphorylation are blocked. The archaea uses cholesterol as an energy substrate. Porphyrin and ALA inhibits sodium potassium ATPase. This increases cholesterol synthesis by acting upon intracellular SREBP. The cholesterol is metabolized to pyruvate and then the GABA shunt pathway for ultimate use in porphyrin synthesis. The porphyrins can self organize and self replicate into macromolecular arrays. The porphyrin arrays behave like an autonomous organism and can have intramolecular electron transport generating ATP. The porphyrin macroarrays can store information and can have quantal perception. The porphyrin macroarrays serves the purpose of archaeal energetics and sensory perception. The Warburg phenotype is associated with metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Low level electromagnetic fields can induce the Warburg phenotype contributing to human disease.

The role of porphyrins and low level electromagnetic fields in regulation of cell functions and neuro-immuno-endocrine integration is discussed. Low levels of EMF fields can induce digoxin synthesis. Protoporphyrin binds to the peripheral benzodiazepine receptor regulating steroid and digoxin synthesis. Increased porphyrin metabolites can contribute to hyperdigoxinemia. Digoxin can modulate the neuro-immuno-endocrine system. Low level of EMF fields can modulate

membrane, nucleic acid and protein structure and function via induction of porphyrin synthesis. Porphyrins can combine with membranes modulating membrane function. Porphyrins can combine with proteins oxidizing their tyrosine, tryptophan, cysteine and histidine residues producing crosslinking and altering protein conformation and function. Porphyrins can complex with DNA and RNA modulating their function. Porphyrin interpolating with DNA can alter transcription and generate HERV expression. Low level of EMF fields through modulation of porphyrin metabolism can produce heme deficiency by inhibiting heme oxygenase and ferrochelatase. Heme deficiency can also result in disease states. Heme deficiency results in deficiency of heme enzymes. There is deficiency of cytochrome C oxidase and mitochondrial dysfunction. The glutathione peroxidase is dysfunctional and the glutathione system of free radical scavenging does not function. The cytochrome P450 enzymes involved in steroid and bile acid synthesis have reduced activity leading to steroid-cortisol and sex hormones as well as bile acid deficiency states. The heme deficiency results in dysfunction of nitric oxide synthase, heme oxygenase and cystathione beta synthase resulting in lack of gasotransmitters regulating the vascular system and NMDA receptor – NO, CO and H_2S. Heme has got cytoprotective, neuroprotective, anti-inflammatory and antiproliferative effects. Heme is also involved in the stress response. Heme deficiency leads to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[3-5]. Low level electromagnetic fields can modulate cell functions and neuro-immuno-endocrine-genetic integration via induction of porphyrin synthesis.

Low level electromagnetic fields via modulating porphyrin metabolism can produce an autonomic neuropathy. Protoporphyrins block acetyl choline transmission producing a vagal neuropathy with sympathetic over activity. Vagal neuropathy results in immune activation, vasospasm and vascular disease. A vagal neuropathy underlines metabolic syndrome-type 2 diabetes mellitus,

CVA and CAD. Low level electromagnetic fields by modulating porphyrin metabolism can induce cell death. Porphyrin induced increased NMDA transmission and free radical injury can contribute to metabolic syndrome x, CVA and CAD. Free radicals can produce mitochondrial PT pore dysfunction. This can lead to cyto C leak and activation of the caspase cascade leading to apoptosis and cell death. Altered porphyrin metabolism has been described in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The increased porphyrin photo-oxidation generated free radicals mediated NMDA transmission can also contribute to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The protoporphyrins binding to mitochondrial benzodiazepine receptors can regulate brain function and cell death[3, 4, 16].

Low level electromagnetic fields by modulating porphyrin metabolism can generate redox stress to regulate cell functions. The porphyrins can undergo photo-oxidation and auto-oxidation generating free radicals. The archaeal porphyrins can produce free radical injury. Free radicals produce NFKB activation, open the mitochondrial PT pore resulting in cell death, produce oncogene activation, activate NMDA receptor and GAD enzyme regulating neurotransmission and generates the Warburg phenotypes activating glycolysis and inhibiting TCA cycle/oxphos. Porphyrins have been related to metabolic syndrome x, CVA and CAD. Low level electromagnetic fields by modulating porphyrin metabolism can regulate cell membrane sodium potassium ATPase. The porphyrins can complex and intercalate with the cell membrane producing sodium potassium ATPase inhibition adding on to digoxin mediated inhibition. Porphyrins can complex with proteins and nucleic acid producing biophoton emission. Low level electromagnetic fields by modulating porphyrin metabolism can regulate DNA, RNA and protein structure and function. Porphyrins complexing with proteins can modulate protein structure and function. Porphyrins complexing with DNA and RNA can modulate transcription and translation. Low

level electromagnetic fields by modulating porphyrin metabolism can regulate mitochondrial function, peripheral benzodiazepine receptor and steroidogenesis. The porphyrin especially protoporphyrins can bind to peripheral benzodiazepine receptors in the mitochondria and modulate its function, mitochondrial cholesterol transport and steroidogenesis. Peripheral benzodiazepine receptor modulation by protoporphyrins can regulate cell death, cell proliferation, immunity and neural functions. Low level electromagnetic fields by modulating porphyrin metabolism and inducing redox stress can regulate enzyme systems. The porphyrin photo-oxidation generates free radicals which can modulate enzyme function. Redox stress modulated enzymes include pyruvate dehydrogenase, nitric oxide synthase, cystathione beta synthase and heme oxygenase. Free radicals can modulate mitochondrial PT pore function. Free radicals can modulate cell membrane function and inhibit sodium potassium ATPase activity. Thus the porphyrins are key regulatory molecules modulating all aspects of cell function[3-5]. Low level of electromagnetic fields by modulating porphyrin metabolism can induce viroidal and HERV expression. There was an increase in free RNA indicating self replicating RNA viroids and free DNA indicating generation of viroid complementary DNA strands by archaeal reverse transcriptase activity. The actinides and porphyrins modulate RNA folding and catalyse its ribozymal action. Digoxin can cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities. Porphyrin photo-oxidation induced redox stress can produce HDAC inhibition. Archaeal pyruvate producing histone deacetylase inhibition and porphyrins intercalating with DNA can produce endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the RNA viroidal complementary DNA into the noncoding region of eukaryotic non coding DNA using HERV integrase as has been described for borna and ebola viruses. The

archaea and viroids can also induce cellular porphyrin synthesis. Bacterial and viral infections can precipitate porphyria. Thus porphyrins can regulate genomic function. The increased expression of HERV RNA can result in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[14, 15].

Low level electromagnetic fields by modulating porphyrin metabolism and generating redox stress can produce immune activation. The porphyrin photo-oxidation can generate free radicals which can activate NFKB. This can produce immune activation and cytokine mediated injury. The increase in archaeal porphyrins can lead to metabolic syndrome x, CVA and CAD. The protoporphyrins binding to mitochondrial benzodiazepine receptors can modulate immune function. Porphyrins can combine with proteins oxidizing their tyrosine, tryptophan, cysteine and histidine residues producing crosslinking and altering protein conformation and function. Porphyrins can complex with DNA and RNA modulating their structure. Porphyrin complexed with proteins and nucleic acids are antigenic and can lead onto autoimmunity in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[3, 4]. Low level electromagnetic fields by modulating porphyrin metabolism and inducing redox stress can produce insulin resistance. The porphyrin photo-oxidation mediated free radical injury can lead to insulin resistance and atherogenesis. Thus archaeal porphyrins can contribute to metabolic syndrome x. Glucose has got a negative effect upon ALA synthase activity. Therefore hyperglycemia may be reactive protective mechanism to increased archaeal porphyrin synthesis. The protoporphyrins binding to mitochondrial benzodiazepine receptors can modulate mitochondrial steroidogenesis and metabolism. Altered porphyrin metabolism has been described in the metabolic syndrome-type 2 diabetes mellitus with CAD and CVA. Porphyrias can lead onto vascular thrombosis[3, 4]. Low level electromagnetic fields by modulating porphyrin metabolism and inducing redox stress/heme deficiency can activate HIF alpha. The porphyrin

photo-oxidation can generate free radicals inducing HIF alpha and produce metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Heme deficiency can lead to activation of HIF alpha and metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The protoporphyrins binding to mitochondrial benzodiazepine receptors can regulate cell proliferation[3, 4]. Low level electromagnetic fields by modulating porphyrin metabolism can regulate prion protein conformation. The porphyrin can combine with prion proteins modulating their conformation. This leads to abnormal prion protein conformation and degradation. Archaeal porphyrins can contribute to prion disease important in metabolic syndrome x, CVA and CAD. Low level electromagnetic fields by modulating porphyrin metabolism can produce redox stress and regulate HERV expression. The porphyrins can also intercalate with DNA producing HERV expression. The HERV particles generated can contribute to the retroviral state important in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[3, 4].

Porphyrins also have evolutionary significance since porphyria is related to Scythian races and contributes to the behavioural and intellectual characteristics of this group of population. Porphyrins can intercalate into DNA and produce HERV expression. HERV RNA can get converted to DNA by reverse transcriptase which can get integrated into DNA by integrase. This tends to increase the length of the non coding region of the DNA. The increase in non coding region of the DNA is involved in primate and human evolution. Thus, increased rates of porphyrin synthesis would correlate with increase in non coding DNA length. The alteration in the length of the non coding region of the DNA contributes to the dynamic nature of the genome. Thus genetic and acquired porphyrias can lead to alteration in the non coding region of the genome. The alteration of the length of the non coding region of the DNA contributes to the racial and individual differences in populations. An increased

length of non coding region as well as increased porphyrin synthesis leads to increased cognitive and creative neuronal function. Porphyrins are involved in quantal perception and regulation of the thalamocorticothalamic pathway of conscious perception. Thus genetic and acquired porphyrias contribute to higher cognitive and creative capacity of certain races. Porphyrias are common among Eurasian Scythian races who have assumed leadership roles in communities and groups. Porphyrins have contributed to human and primate evolution[3, 4]. The increased porphyrin synthesis in the Scythian races contributes to higher level of extrasensory quantal perception in this racial group. This contributes to higher level of cognitive and spiritual function of the brain in this racial group. These racial groups have increase incidence of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

The porphyrins can contribute to the role of low level electromagnetic fields in the pathogenesis of metabolic syndrome x, CVA and CAD. An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states-metabolic syndrome-type 2 diabetes mellitus, CVA and CAD is described. Archaeal porphyrin synthesis and induction of endogenous porphyrin synthesis is crucial in the pathogenesis of these disorders. Porphyrins may serve as regulatory molecules modulating immune, neural, endocrine, metabolic and genetic systems. The porphyrins photo-oxidation generated free radicals can produce immune activation, produce cell death, activate cell proliferation, produce insulin resistance and modulate conscious/quantal perception. Porphyrins can regulate hemispheric dominance. The archaeal porphyrins functions as key regulatory molecules with mitochondrial benzodiazepine receptors playing an important role. Thus the porphyrins contributes to the inducing role of low level electromagnetic fields in the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Low level electromagnetic fields and its porphyrin messengers can regulate immune,

neural, endocrine, metabolic and genetic systems[3, 4]. A hypothesis regarding the role of porphyrins and quantal perception as well as the role of porphyrins in environmental communication/modulation of digital information storage/processing system is presented. Thus porphyrin microarrays can function as a quantal computer mediating extrasensory perception. Porphyrin microarrays in human systems and brain owing to the wave particle nature of porphyrins can bridge the quantal world and particulate world. The relationship between low level of electromagnetic fields and human disease is highlighted.

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Actinidic Archaea Mediates Biological Transmutation in Human Systems – Role in Metabolic Syndrome-Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke

Introduction

Biological transmutation has been postulated by several groups of workers in microbial systems[1, 2]. Quantizing structures of optimal size and shape are necessary for non barrier nuclear interactions. The situation is realized in microbial cultures. During the growth process, the replication of DNA and other biomacromolecules takes place. In the region of growth, the interatomic potential holes with slowly changing sizes are constantly appearing and in this situation non barrier nuclear interactions can take place. Actinidic archaea has been described in human systems from our laboratory and function as cellular endosymbionts regulating multiple cellular functions. The actinidic archaea utilizes an alternate biochemistry depended on actinides for enzyme catalysis. The seashores of Kerala are rich in actinidic elements present as rutile, illmenite and monazite. The actinidic archaea is an endosymbiont of the human cell and it is possible that the organism can mediate biological transmutation. Transmutation of magnesium to calcium can serve as a mechanism of regulation of the neuro-immuno-endocrine system. Deficiency of magnesium is seen in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[3]. The actinidic archaea can exist as nanoarchaea which can undergo magnetite and calcium mineralization. It is possible that magnesium is being transmuted biologically to calcium to produce amounts sufficient for calcium mineralization. Calcified nanoarchaea can produce a systemic immune activation contributing to the diverse pathologies of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD to study biological transmutation of magnesium to calcium and cerium. The results are presented in this paper.

Materials and Methods

Informed consent was obtained from all patients included in the study. The permission of the Ethics Committee of the Institute was obtained. Fasting blood was drawn for the study from normal individuals without any systemic disease.

Experimental system was as follows: The basic system contained patient's serum 0.5 ml + normal serum 0.25 ml + physiological buffered saline + cerium chloride 0.1 mg/ml. To the basic system $MgSO_4$ 0.1 mg/ml was added.

The Mg^{++} and Ca^{++} were estimated at 0 hour. The remaining portion was incubated for 16 hours at 37 ℃ for 16 hours. The Mg^{++} and Ca^{++} were estimated at the end of 16 hours. The estimation of Mg^{++} and Ca^{++} were done by using commercial kits. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm).

Results

The results showed that there was a decrease in magnesium and a concomitant increase in calcium in incubated serum samples from normal individuals. The percentage decrease in magnesium was 15.68 to 31.48%. The percentage increase in calcium was 10.43 to 9.79%. There was detection of cytochrome F420 in the system by fluorescence indicating archaeal growth dependent on actinidic cerium. This showed that the actinidic archaea was mediating the biological transmutation of magnesium to calcium.

Table 1 *Experimental biological transmutation.*

Case	Time	Mg (mEq/l)	% change in Mg	Ca (ng/dl)	% change in Ca
Case 1	0 hr	1.415		0.796	
	16 hrs	1.193	15.68 ↓	8.310	10.43 ↑
Case 2	0 hr	2.290		0.764	
	16 hrs	1.569	31.48 ↓	7.480	9.79 ↑

Discussion

The results showed that there is biological transmutation of magnesium to calcium in human systems mediated by actinidic archaea dependent on cerium for its growth. Regulation of calcium and magnesium levels in the cell by archaeal mediated biological transmutation can regulate multiple physiological systems. Calcium can modulate the mitochondrial PT pore and cell death. Cellular calcium levels are also involved in oncogene activation. Magnesium levels in the cell can regulate glycosylation and protein processing modulating golgi body and lysosomal function. Presynaptic calcium levels can regulate synaptic transmission as well as neurotransmitter release into the synapse. Cellular calcium levels can activate NFKB producing immune activation. Magnesium and calcium levels can modulate mitochondrial function and metabolism[3]. This can contribute to the pathogenesis of type 2 diabetes mellitus with CAD and CVA.

There is magnesium depletion from the system and calcium accumulation which can predispose to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[3]. The increased intracellular calcium can open up the mitochondrial PT pore producing a mitochondrial dysfunction. Magnesium deficiency can produce a mitochondrial ATP synthase defect. The opening of the mitochondrial PT pore produces volume dysregulation of the mitochondria, hyperosmolarity and expansion of the mitochondrial matrix space producing

outer membrane rupture. This leads to release of cytochrome C into the cytoplasm, activating the caspase cascade and cell death. Mitochondrial dysfunction and related apoptosis as well as free radical generation has been related to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Decreased intracellular magnesium can lead to altered glyconjugate synthesis and a protein processing dysfunction. Protein processing golgi body dysfunction as well as ER stress has been related to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Altered cell surface glyconjugates can lead to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Altered glyconjugates can lead to defective MHC antigen presenting pathway and autoimmunity in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Increased calcium within the presynaptic neuron can lead to increased glutamate release into the synapse and increased postsynaptic neuronal calcium can increase the NMDA signal transduction. Increased NMDA signal transduction can contribute to metabolic syndrome x, CVA and CAD. A decrease in intracellular magnesium can block the phosphorylation reaction involved in protein tyrosine kinase receptor activity leading to insulin resistance and metabolic syndrome-type 2 diabetes mellitus with CAD and CVA. An increase in intracellular calcium can activate the NFKB signal transduction producing immune activation and autoimmunity in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Immune activation has also been related to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

A calcium excess related PT pore dysfunction of mitochondria can generate free radicals. Free radicals can produce apoptosis, immune activation, insulin resistance and NMDA activity. Free radicals can activate NFKB producing immune activation and autoimmunity in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Free radicals can produce mitochondrial dysfunction and cell death. Free radicals can activate HIF alpha. Free radicals can thus

produce insulin resistance and metabolic syndrome-type 2 diabetes mellitus with CAD and CVA.

A shadow biosphere of actinidic archaea has been described in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The archaea transmutates magnesium to calcium for the purpose of biological mineralisation. The archaea can exist as nanoarchaea which can get calcified to form calcified nanoarchaeal forms. Calcified nanoarchaeal particles can induce NFKB. This can produce a state of systemic immune activation. This activates the AKT PI3 cascade inducing the Warburg phenotype with anaerobic glycolysis which is the basis of most human disease. The lymphocytes depend of glycolysis for its energy needs. Increased glycolysis can lead to immune activation. Immune activation is important in the pathogenesis of metabolic syndrome x, CVA and CAD. The glycolysis generated NADPH activates the NOX enzyme important in insulin receptor function and NMDA activity. Thus the creation of Warburg phenotype can produce metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

Thus the transmutation related free radical generation and altered calcium-magnesium ratios in the cell can alter synaptic transmission, mitochondrial function, golgi body/ER function, lysosomal function, immune activation, cell proliferation, insulin resistance and cell death. The actinidic archaea related biological transmutation is an important regulatory mechanism of the cell whose dysfunction can produce altered neuro-immune-endocrine regulation. This can lead to human disease. The biological transmutation gives the actinidic archaea energy to survive and generates calcium for its biological mineralisation.

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Endosymbiotic Archaeal Generated RNA Viroids Can Regulate Cell Function and Contribute to Metabolic Syndrome-Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke

Introduction

Actinides like rutile producing intracellular magnesium deficiency due to rutile-magnesium exchange sites in the cell membrane has been implicated in the etiology of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[1, 2]. Organisms like phytoplasmas and viroids have also been demonstrated to play a role in the etiology of these diseases[3, 4]. RNA viroids could contribute to the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[2]. The possibility of generation of RNA viroids by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered[5-8]. An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described[6]. The role of RNA viroids generated by actinidic archaea in regulation of body functions and the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD is discussed.

Materials and Methods

Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The following groups were included in the study: – metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as

described by Richmond[10]. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ^{o}C for 1 hour. The following estimations were carried out: – Cytochrome F420, free RNA and free DNA[11-14]. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). The statistical analysis was done by ANOVA.

Results

The parameters checked as indicated above were: – cytochrome F420, free RNA and free DNA. Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-2 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1 *Effect of rutile and antibiotics on cytochrome F420.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**
Normal	4.48	0.15	18.24	0.66
DM	22.59	1.86	57.05	8.45
CVA	22.29	1.66	59.02	7.50
CAD	22.06	1.61	57.81	6.04
F value	306.749		130.054	
P value	< 0.001		< 0.001	

Table 2 *Effect of rutile and antibiotics on free RNA and DNA.*

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy+Cipro)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
DM	23.01	1.67	65.35	3.56	23.33	1.86	66.46	3.65
CVA	22.56	2.46	62.70	4.53	23.32	1.74	65.67	4.16
CAD	23.30	1.42	65.07	4.95	23.11	1.52	66.68	3.97
F value	337.577		356.621		427.828		654.453	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[15, 16]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[17, 18]. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[19]. This can contribute to the pathogenesis of type 2 diabetes mellitus with CAD and CVA.

There was an increase in free RNA indicating self replicating RNA viroids and free DNA indicating generation of viroid complementary DNA strands by archaeal reverse transcriptase activity. The actinides modulate RNA folding and catalyse its ribozymal action. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities[20]. Archaea induced immune activation and redox stress can produce histone deacetylase inhibition resulting in endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the RNA viroidal complementary DNA into the noncoding region of eukaryotic non coding DNA

using HERV integrase as has been described for borna and ebola viruses[21]. The noncoding DNA is lengthened by integrating RNA viroidal complementary DNA with the integration going on as a continuing event. The archaea genome can also get integrated into human genome using integrase as has been described for trypanosomes[22]. The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites[21, 22]. This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters[23]. The viroidal complementary DNA can function as jumping genes producing a dynamic genome important in storage of synaptic information, HLA gene expression and developmental gene expression. The RNA viroids can regulate mRNA function by RNA interference[20]. The phenomena of RNA interference can modulate T cell and B cell function, insulin signaling lipid metabolism, cell growth and differentiation, apoptosis, neuronal transmission and euchromatin/heterochromatin expression. This can contribute to the pathogenesis of type 2 diabetes mellitus with CAD and CVA.

The RNA viroids and its complementary DNA developed into cholesterol enveloped RNA and DNA viruses like herpes, retrovirus, influenza virus, borna virus, cytomegalo virus and Ebstein Barr virus by recombining with archaeal, eukaryotic and human genes resulting in viral speciation[24, 25, 26]. The RNA viroids can also recombine with endogenous commensal RNA and DNA viruses producing speciation. Viral species are ill defined and fuzzy with all of them forming one common genetic pool with frequent horizontal gene transfer and recombination. Thus the multi and unicellular eukaryote with its genes serves the purpose of viral speciation. This can contribute to the pathogenesis of type 2 diabetes mellitus with CAD and CVA.

The multicellular eukaryotes are like archaeal biofilms. The archaea with a mevalonate pathway uses the extracellular RNA viroids for quorum sensing and

in the generation of symbiotic biofilm like structures which develop into multicellular eukaryotes[27, 28]. The endosymbiotic archaea and bacteria with mevalonate pathway still uses the RNA viroids for the regulation of muticellular eukaryote. Pollution is induced by the primitive nanoarchaea and mevalonate pathway bacteria synthesized PAH and methane leading on to redox stress. Redox stress leads to sodium potassium ATPase inhibition, inward movement of plasma membrane cholesterol, defective SREBP sensing, increased cholesterol synthesis and nanoarchaeal/mevalonate pathway bacterial growth[29]. Redox stress leads on to viroidal and archaeal multiplication. Redox stress can also lead to HERV reverse transcriptase and integrase expression. The noncoding DNA is formed of integrating RNA viroidal complementary DNA and archaea with the integration going on as a continuing event. The archaeal pox like dsDNA virus forms evolutionarily the nucleus. The integrated viroidal, archaeal and mevalonate pathway bacterial sequences can undergo vertical transmission and can exist as genomic parasites. The genomic integrated archaea, mevalonate pathway bacteria and viroids form a genomic reserve of bacteria and viruses which can recombine with human and eukaryotic genes producing bacterial and viral speciation. The change in the length and grammar of the noncoding region produces eukaryotic speciation and individuality[30]. The integration of nanoarchaea, mevalonate pathway prokaryotes and viroids in to the eukaryotic and human genome produces a chimera which can multiply producing biofilm like multicellular structures having a mixed archaeal, viroidal, prokaryotic and eukaryotic characters which is a regression from the multicellular eukaryotic tissue. This results in a new neuronal, metabolic, immune and tissue phenotype leading to human disease. This produces infection related metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

Archaea and RNA viroid can bind the TLR receptor induce NFKB producing immune activation and cytokine TNF alpha secretion[2, 32]. The archaea and

viroid induced chronic immune activation and generation of superantigens can lead on to autoimmunity in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Archaea and viroids can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype[33]. The increased glycolytic hexokinase activity, decrease in blood ATP, leakage of cytochrome C, increase in serum pyruvate and decrease in acetyl CoA indicates the generation of the Warburg phenotype. There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics and metabolic syndrome. The archaea and viroid generated cytokines can lead to TNF alpha induced insulin resistance and metabolic syndrome x. The accumulated pyruvate enters the GABA shunt pathway and is converted to citrate which is acted upon by citrate lyase and converted to acetyl CoA, used for cholesterol synthesis[33]. The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy needs. The increased cholesterol substrate leads to increased archaeal growth and digoxin synthesis leading to metabolic channeling to the mevalonate pathway[34]. The archaea and viroid induced monocyte activation and Warburg phenotype induced increased cholesterol synthesis leads to atherogenesis. Viroid induced RNA interference can modulate the mRNAs concerned with insulin receptor function and lipid metabolism contributing to metabolic syndrome-type 2 diabetes mellitus with CAD and CVA. The RNA viroids can recombine with HERV sequences and get encapsulated in microvesicles contributing to the retroviral state. The prion protein conformation is modulated by RNA viroid binding producing prion disease. Human endogenous retroviruses and prions have been related to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

Thus the actinidic archaea generated RNA viroids can regulate cell function and produce neuro-immuno-genetic-endocrine-metabolic integration. The RNA viroids and their complementary DNA can serve the purpose of viral speciation.

The RNA viroids also contributes to the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

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Endosymbiotic Actinidic Archaeal Cholesterol Catabolic Syndrome – Hypocholesterolemia and Metabolic Syndrome-Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke

Introduction

Actinidic archaea have been implicated in the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[1-9]. Actinide based primitive organism like archaea have a mevalonate pathway and cholesterol catabolism. Cholesterol catabolism by actinidic archaea can lead to cholesterol depletion and a hypocholesterolemic state contributing to the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[10-17].

Archaea can use cholesterol as a carbon and energy source. Archaeal cholesterol catabolism can lead to multiple systemic diseases. Low cholesterol values in populations have been related to high mortality. The archaeal cholesterol catabolising enzymes were studied and the results in presented in this paper. This can be described as the endosymbiotic actinidic archaeal cholesterol catabolic syndrome[10-17].

Materials and Methods

The following groups were included in the study: – metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond[18]. Aliquots were withdrawn at zero time immediately after mixing and after

incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420, polycyclic aromatic hydrocarbon, digoxin, bile acid, cholesterol oxidase activity measured by hydrogen peroxide liberation, pyruvate, butyrate and propionate were estimated[19-21]. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Polycyclic aromatic hydrocarbon was estimated by measuring hydrogen peroxide liberated by using glucose reagent. Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-4 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1 *Effect of rutile and antibiotics on cytochrome F420 and PAH.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66	4.45	0.14	18.25	0.72
DM	22.59	1.86	57.05	8.45	23.40	1.55	65.77	5.27
CVA	22.29	1.66	59.02	7.50	23.23	1.97	65.89	5.05
CAD	22.06	1.61	57.81	6.04	23.46	1.91	61.56	4.61
	F value 306.749 P value < 0.001		F value 130.054 P value < 0.001		F value 391.318 P value < 0.001		F value 257.996 P value < 0.001	

Table 2 *Effect of rutile and antibiotics on butyrate and propionate generation from cholesterol.*

Group	Butyrate % change (Increase with Rutile)		Butyrate % change (Decrease with Doxy+Cipro)		Propionate % change (Increase with Rutile)		Propionate % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.43	0.19	18.13	0.63	4.40	0.10	18.48	0.39
DM	23.27	1.53	58.91	6.09	22.87	1.84	66.31	3.68
CVA	23.32	1.71	63.15	7.62	23.45	1.79	66.32	3.63
CAD	22.86	1.91	63.66	6.88	23.17	1.88	68.53	2.65
	F value 380.721 P value < 0.001		F value 171.228 P value < 0.001		F value 372.716 P value < 0.001		F value 556.411 P value < 0.001	

Table 3 *Effect of rutile and antibiotics on digoxin and bile acids.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		Bile acids % change (Increase with Rutile)		Bile acids % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	0.11	0.00	0.054	0.003	4.29	0.18	18.15	0.58
DM	0.47	0.04	0.202	0.025	22.87	2.58	64.51	5.93
CVA	0.56	0.05	0.220	0.052	22.29	1.47	64.35	5.58
CAD	0.53	0.06	0.212	0.045	23.30	1.88	62.49	7.26
	F value 135.116 P value < 0.001		F value 71.706 P value < 0.001		F value 290.441 P value < 0.001		F value 203.651 P value < 0.001	

Table 4 *Effect of rutile and antibiotics on pyruvate and hydrogen peroxide.*

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy+Cipro)		H_2O_2 % (Increase with Rutile)		H_2O_2 % (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.34	0.21	18.43	0.82	4.43	0.19	18.13	0.63
DM	20.67	1.38	58.75	8.12	23.27	1.53	58.91	6.09
CVA	21.21	2.36	58.73	8.10	23.32	1.71	63.15	7.62
CAD	21.07	1.79	63.90	7.13	22.86	1.91	63.66	6.88
	F value 321.255 P value < 0.001		F value 115.242 P value < 0.001		F value 380.721 P value < 0.001		F value 171.228 P value < 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[22-24]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[22-24]. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis and archaeal cholesterol hydroxylase activity indicating bile acid synthesis were increased[22-24]. The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide[22-24]. The pyruvate gets converted to glutamate and ammonia by the GABA shunt pathway. The archaeal aromatization of cholesterol generating PAH was also detected[22-24]. This indicates archaeal cholesterol aromatase activity. The archaeal cholesterol side chain oxidase activity generates butyrate and propionate. Thus archaeal cholesterol oxidase, cholesterol aromatase, cholesterol side chain oxidase, cholesterol hydroxylase and beta hydroxyl steroid dehydrogenase activity were detected in high levels in the patient population of metabolic syndrome-type 2 diabetes mellitus, CVA and

CAD. The archaeal cholesterol catabolising enzymes were actinide dependent. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[25]. This leads to a cholesterol depleted state and hypocholesterolemic syndrome in patients with metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

Low cholesterol has been related to metabolic syndrome x, CVA and CAD. Low cholesterol is detected in patients with autism and schizophrenia[10-17]. The gut endotoxins and lipopolysaccharides are absorbed along with fat producing the syndrome of metabolic endotoxaemia. The endotoxins and lipopolysaccharides can combine with lipoproteins and are detoxified. Metabolic endotoxaemia produces chronic immune activation and generation of superantigens. This has been related to the genesis of autoimmune disease. Metabolic endotoxaemia results in immune activation and generation of TNF alpha which modulates the insulin receptor producing insulin resistance. Insulin resistance is related to metabolic syndrome-type 2 diabetes mellitus and vascular thrombosis. Metabolic endotoxaemia related chronic immune activation drives the retroviral state and HERV sequences have been related to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Metabolic endotoxaemia can induce NFKB which can lead to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Thus hypocholesterolemia leads to non-detoxification of endotoxins and lipopolysaccharides resulting in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[10-17].

Infections have been related to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Gut bacteria with increase in gut firmicutes and decrease in bacteroides have been related to metabolic syndrome-type 2 diabetes mellitus with CAD and CVA. Chlamydial infections have been related to vascular

disease. Low cholesterol leads to lack of lipoprotein binding to endotoxins[10-17]. The endotoxins and lipopolysaccharides are not detoxified.

Viral diseases have been related to the pathogenesis of metabolic syndrome x, CVA and CAD. The virus binds to lipid microdomains in the cell membrane. Cholesterol depletion leads to alteration in lipid microdomains and increased entry of virus in the cell. Retroviral infection-exogenous and endogenous have been related to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. CMV infection and herpes infection has been related to atherogenesis. Prion disease has been related to alterations in cholesterol metabolism. Thus a cholesterol depleted state can lead to increased predilection to viral infection and metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[10-17].

The actinidic archaea uses cholesterol catabolism to generate energy. The cholesterol catabolizing enzymes of the archaea are dependent on actinides. The archaeal cholesterol catabolism leads to a cholesterol depleted state and the genesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Cholesterol depleted state have been related to high mortality. This can be described as the endosymbiotic actinidic archaeal cholesterol catabolic syndrome[10-17].

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Endosymbiotic Actinidic Archaeal Mediated Warburg Phenotype Mediates Metabolic Syndrome-Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke

Introduction

Actinides like rutile as well as organisms like phytoplasmas and viroids have been implicated in the etiology of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[1, 2, 3, 4]. The Warburg phenotype has been related to the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[4]. The possibility of Warburg phenotype induced by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered in this paper[5-8]. An actinide dependent shadow biosphere of archaea and viroids in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD is described[7, 9].

Materials and Methods

The following groups were included in the study: – metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond[10]. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420 and hexokinase[11-13]. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Informed consent of the

subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-2 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1 *Effect of rutile and antibiotics on cytochrome F420.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**
Normal	4.48	0.15	18.24	0.66
DM	22.59	1.86	57.05	8.45
CVA	22.29	1.66	59.02	7.50
CAD	22.06	1.61	57.81	6.04
F value	306.749		130.054	
P value	< 0.001		< 0.001	

Table 2 *Effect of rutile and antibiotics on hexokinase.*

Group	Hexokinase % change (Increase with Rutile)		Hexokinase % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD
Normal	4.21	0.16	18.56	0.76
DM	23.23	1.88	65.11	5.14
CVA	21.11	2.25	64.20	5.38
CAD	22.47	2.17	65.97	4.62
F value	292.065		317.966	
P value	< 0.001		< 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[6, 14]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[15, 16]. The archaeal glycolytic hexokinase activity were increased. The part of the increased glycolytic hexokinase activity detected is human. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[17]. This can contribute to the pathogenesis of type 2 diabetes mellitus with CAD and CVA.

Archaea can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype[18]. The increased glycolytic hexokinase activity indicates the generation of the Warburg phenotype. The generation of the Warburg phenotype is due to activation of HIF alpha. This stimulates anaerobic glycolysis, inhibits pyruvate dehydrogenase, inhibits mitochondrial oxidative phosphorylation, stimulates heme oxygenase, stimulates VEGF and activates nitric oxide synthase. This can lead to increased

cell proliferation and malignant transformation. The mitochondrial PT pore hexokinase is increased leading onto cell proliferation. There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics and metabolic syndrome. The archaea and viroid generated cytokines can lead to TNF alpha induced insulin resistance and metabolic syndrome-type 2 diabetes mellitus with CAD and CVA. The increase in the glycolytic enzyme fructose 1, 6 diphosphatase increases the pentose phosphate pathway. This generates NADPH which activates NOX. NOX activation is related to NMDA activation and glutamate excitotoxicity. This leads onto metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[18].

The increase in glycolysis activates the enzyme fructose 1, 6 diphosphatase which activates the pentose phosphate pathway liberating NADPH. This increases NOX activity generating free radical stress and H_2O_2. Free radical stress is related to insulin resistance and metabolic syndrome x. Free radicals can activate NFKB producing immune activation and autoimmunity in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Free radicals can open the mitochondrial PT pore, produce release of cyto C and activate the caspase cascade. This produces metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Free radicals can produce HDAC inhibition and HERV generation. The encapsulation of HERV particles in phospholipids vesicles can mediate the generation of HERV sequences important in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Free radicals can also promote atherogenesis[18].

The lymphocytes depend on glycolysis for its energy needs. The increase in glycolysis owing to the induction of Warburg phenotype can lead to immune activation. Immune activation can lead to autoimmunity in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. TNF alpha can activate the NMDA receptor leading to glutamate excitotoxicity important in metabolic syndrome-

type 2 diabetes mellitus, CVA and CAD. TNF alpha can induce expression of HERV particles contributing to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. TNF alpha can also act upon the insulin receptor producing insulin resistance. NOX activation consequent to the generation of the Warburg phenotype also activates the insulin receptor. Thus there is a hyperinsulinemic state leading on to metabolic syndrome-type 2 diabetes mellitus with CAD and CVA[18].

Thus the induction of the Warburg phenotype can lead to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The Warburg phenotype leads to inhibition of pyruvate dehydrogenase and accumulation of pyruvate. The accumulated pyruvate enters the GABA shunt pathway and is converted to citrate which is acted upon by citrate lyase and converted to acetyl CoA, used for cholesterol synthesis. The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy needs. The increased cholesterol substrate leads to increased archaeal growth and further induction of the Warburg phenotype[18].

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Endosymbiontic Actinidic Archaeal Synthesis of Digoxin from Cholesterol Regulates Cellular Function and Contributes to Metabolic Syndrome-Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke

Introduction

Actinides like rutile, endogenous digoxin as well as organisms like phytoplasmas and viroids have been implicated in the etiology of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[1-4]. Endogenous digoxin has been related to the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[4]. The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered[5-8]. An actinide dependent shadow biosphere of archaea in the above mentioned disease states is described[7, 9].

Materials and Methods

The following groups were included in the study: – metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond[10]. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420 and digoxin[11-13]. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Informed consent of the

subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-2 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

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Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**
Normal	4.48	0.15	18.24	0.66
DM	22.59	1.86	57.05	8.45
CVA	22.29	1.66	59.02	7.50
CAD	22.06	1.61	57.81	6.04
F value	306.749		130.054	
P value	< 0.001		< 0.001	

Table 2 *Effect of rutile and antibiotics on digoxin.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**
Normal	0.11	0.00	0.054	0.003
DM	0.47	0.04	0.202	0.025
CVA	0.56	0.05	0.220	0.052
CAD	0.53	0.06	0.212	0.045
F value	135.116		71.706	
P value	< 0.001		< 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[6, 14]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[15, 16]. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis was increased[8]. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[17]. This can contribute to the pathogenesis of type 2 diabetes mellitus with CAD and CVA.

Archaeal digoxin induced redox stress can produce histone deacetylase inhibition resulting in endogenous retroviral (HERV) reverse transcriptase and integrase expression. Digoxin can cut and paste the HERV RNA by modulating RNA splicing generating RNA viroidal diversity[18]. This can also integrate the HERV RNA complementary DNA into the noncoding region of eukaryotic non coding DNA using HERV integrase[19]. The noncoding DNA is lengthened by integrating HERV RNA complementary DNA with the integration going on as a

continuing event. The archaea genome can also get integrated into human genome using integrase as has been described for trypanosomes[20]. The integrated archaea can undergo vertical transmission and can exist as genomic parasites[19, 20]. This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters as well as eukaryotic speciation and individuality[21]. The HERV RNA complementary DNA can function as jumping genes producing a dynamic genome important in storage of synaptic information, HLA gene expression and developmental gene expression. The HERV RNA can regulate mRNA function by RNA interference[18]. The phenomena of RNA interference can modulate T cell and B cell function, insulin signaling lipid metabolism, cell growth and differentiation, apoptosis, neuronal transmission and euchromatin/ heterochromatin expression. This can lead to the genesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

Digoxin induced calcium oscillations can activate NFKB producing immune activation and cytokine secretion. The archaeal digoxin induced chronic immune activation can lead on to autoimmunity in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[23]. Archaeal digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype[24]. There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics and metabolic syndrome. The archaeal digoxin generated cytokines can lead to TNF alpha induced insulin resistance and metabolic syndrome x. Digoxin induced sodium potassium ATPase inhibition can lead to increase in HMG CoA reductase activity and increased cholesterol synthesis. The increased cholesterol substrate also leads to increased archaeal growth and digoxin synthesis due to metabolic channeling to the mevalonate pathway. Digoxin can produce sodium-potassium ATPase inhibition and inward movement of plasma membrane cholesterol. This produces defective SREBP sensing, increased HMG CoA reductase activity and cholesterol synthesis.

The digoxin induced inward movement of plasma membrane cholesterol can alter membrane cholesterol/sphingomyelin ratio producing modified lipid microdomains. The digoxin induced lipid microdomain modulation can regulate the GPCR couple adrenaline, noradrenaline, glucagon and neuropeptide receptors as well as protein tyrosine kinase linked insulin receptor. The digoxin mediated inhibition of nuclear membrane sodium-potassium ATPase can modulate nuclear membrane lipid microdomains and steroidal/thyroxine DNA receptor function. Thus endogenous digoxin can modulate all the endocrine receptors by regulating lipid microdomains. Hyperdigoxinemia is important in the pathogenesis of atherogenesis and metabolic syndrome-type 2 diabetes mellitus with CAD and CVA. Digoxin induced sodium-potassium ATPase inhibition results in an ATP sparing effect. Eighty percent of the ATP generated is used to run the sodium-potassium ATPase pump. The digoxin inhibition of the sodium-potassium ATPase spares this ATP which is then used for lipid synthesis. Thus endogenous digoxin and the shadow biosphere generated Warburg phenotype can produce increased lipid synthesis and obesity important in metabolic syndrome-type 2 diabetes mellitus with CAD and CVA. Fat fuels insulin resistance by binding to the toll receptor and producing immune activation and immune infiltration of the adipose tissue. The archaeal digoxin induced monocyte activation and Warburg phenotype induced increased cholesterol synthesis leads to atherogenesis. The digoxin induced increased intracellular calcium can lead to PT pore dysfunction and contributes to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[4]. The digoxin mediated transcribed HERV RNA can get encapsulated in microvesicles contributing to the retroviral state. The prion protein conformation is modulated by HERV RNA binding producing prion disease. Prions and HERV sequences are related to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Thus the archaeal digoxin can produce neuro-immune-metabolic-endocrine-genetic integration. The increased archaeal cholesterol catabolism and

digoxin secretion can lead to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

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Archaeal Porphyrins, Regulation of Cell Function and Neuro-Immuno-Endocrine Integration – Relation to Metabolic Syndrome-Type 2 Diabetes Mellitus with Coronary Artery Disease and Stroke

Introduction

Actinidic archaea have been related to the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[1-8]. An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described[7, 9]. Actinidic archaea have a mevalonate pathway and are cholesterol catabolizing. They can use cholesterol as a carbon and energy source. Archaeal cholesterol catabolism can generate porphyrins via the cholesterol ring oxidase generated pyruvate and GABA shunt pathway. Porphyrins have been related to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The role of archaeal porphyrins in regulation of cell functions and neuro-immuno-endocrine integration is discussed.

Materials and Methods

The following groups were included in the study: – metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond[10]. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ^{o}C for 1 hour. The following estimations were carried out: – Cytochrome F420, free RNA, free DNA, polycyclic aromatic hydrocarbon, hydrogen peroxide, pyruvate,

ammonia, glutamate, delta aminolevulinic acid, succinate, glycine and digoxin[11-13]. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Polycyclic aromatic hydrocarbon was estimated by measuring hydrogen peroxide liberated by using glucose reagent. Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-6 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time. There was upregulated archaeal porphyrin synthesis in the patient population which was archaeal in origin as indicated by actinide catalysis of the reactions. The cholesterol oxidase pathway generated pyruvate which entered the GABA shunt pathway. This resulted in synthesis of succinate and glycine which are substrates for ALA synthase.

Table 1 *Effect of rutile and antibiotics on cytochrome F420 and PAH.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66	4.45	0.14	18.25	0.72
DM	22.59	1.86	57.05	8.45	23.40	1.55	65.77	5.27
CVA	22.29	1.66	59.02	7.50	23.23	1.97	65.89	5.05
CAD	22.06	1.61	57.81	6.04	23.46	1.91	61.56	4.61
	F value 306.749 P value < 0.001		F value 130.054 P value < 0.001		F value 391.318 P value < 0.001		F value 257.996 P value < 0.001	

Table 2 *Effect of rutile and antibiotics on free RNA and DNA.*

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy+Cipro)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
DM	23.01	1.67	65.35	3.56	23.33	1.86	66.46	3.65
CVA	22.56	2.46	62.70	4.53	23.32	1.74	65.67	4.16
CAD	23.30	1.42	65.07	4.95	23.11	1.52	66.68	3.97
	F value 337.577 P value < 0.001		F value 356.621 P value < 0.001		F value 427.828 P value < 0.001		F value 654.453 P value < 0.001	

Table 3 *Effect of rutile and antibiotics on digoxin and delta aminolevulinic acid.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		ALA % (Increase with Rutile)		ALA % (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	0.11	0.00	0.054	0.003	4.40	0.10	18.48	0.39
DM	0.47	0.04	0.202	0.025	22.87	1.84	66.31	3.68
CVA	0.56	0.05	0.220	0.052	23.45	1.79	66.32	3.63
CAD	0.53	0.06	0.212	0.045	23.17	1.88	68.53	2.65
	F value 135.116 P value < 0.001		F value 71.706 P value < 0.001		F value 372.716 P value < 0.001		F value 556.411 P value < 0.001	

Table 4 *Effect of rutile and antibiotics on succinate and glycine.*

Group	Succinate % (Increase with Rutile)		Succinate % (Decrease with Doxy+Cipro)		Glycine % change (Increase with Rutile)		Glycine % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.41	0.15	18.63	0.12	4.34	0.15	18.24	0.37
DM	23.70	1.75	68.06	3.52	23.81	1.49	64.89	6.01
CVA	23.66	1.67	65.97	3.36	23.09	1.81	65.86	4.27
CAD	22.92	2.14	67.54	3.65	21.93	2.29	63.70	5.63
	F value 403.394 P value < 0.001		F value 680.284 P value < 0.001		F value 348.867 P value < 0.001		F value 364.999 P value < 0.001	

Table 5 *Effect of rutile and antibiotics on pyruvate and Glutamate.*

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy+Cipro)		Glutamate (Increase with Rutile)		Glutamate (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.34	0.21	18.43	0.82	4.21	0.16	18.56	0.76
DM	20.67	1.38	58.75	8.12	23.23	1.88	65.11	5.14
CVA	21.21	2.36	58.73	8.10	21.11	2.25	64.20	5.38
CAD	21.07	1.79	63.90	7.13	22.47	2.17	65.97	4.62
	F value 321.255 P value < 0.001		F value 115.242 P value < 0.001		F value 292.065 P value < 0.001		F value 317.966 P value < 0.001	

Table 6 *Effect of rutile and antibiotics on hydrogen peroxide and ammonia.*

Group	H_2O_2 % (Increase with Rutile)		H_2O_2 % (Decrease with Doxy+Cipro)		Ammonia % (Increase with Rutile)		Ammonia % (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.43	0.19	18.13	0.63	4.40	0.10	18.48	0.39
DM	23.27	1.53	58.91	6.09	22.87	1.84	66.31	3.68
CVA	23.32	1.71	63.15	7.62	23.45	1.79	66.32	3.63
CAD	22.86	1.91	63.66	6.88	23.17	1.88	68.53	2.65
	F value 380.721 P value < 0.001		F value 171.228 P value < 0.001		F value 372.716 P value < 0.001		F value 556.411 P value < 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[6, 14]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[15]. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis[8]. The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide[14]. The pyruvate gets converted to glutamate and ammonia by the GABA shunt pathway. The pyruvate is converted to glutamate by serum glutamate pyruvate transaminase. The glutamate gets acted upon by glutamate dehydrogenase to generate alpha ketoglutarate and ammonia. Alanine is most commonly produced by the reductive amination of pyruvate via alanine transaminase. This reversible reaction involves the interconversion of alanine and pyruvate, coupled to the interconversion of alpha-ketoglutarate (2-oxoglutarate) and glutamate. Alanine can contribute to glycine. Glutamate is acted upon by Glutamic acid decarboxylase to generate GABA. GABA is converted to succinic semialdehyde by GABA transaminase. Succinic semialdehyde is converted to succinic acid by succinic semialdehyde dehydrogenase. Glycine combines with succinyl CoA to generate delta aminolevulinic acid catalysed by the enzyme ALA synthase. There was upregulated archaeal porphyrin synthesis in the patient population which was archaeal in origin as indicated by actinide catalysis of the reactions. The cholesterol oxidase pathway generated pyruvate which entered the GABA shunt pathway. This resulted in synthesis of succinate and glycine which are substrates for ALA synthase. The archaea can undergo magnetite and calcium carbonate

mineralization and can exist as calcified nanoforms[16, 17]. This can lead to the pathogenesis of type 2 diabetes mellitus with CAD and CVA.

There was an increase in free RNA indicating self replicating RNA viroids and free DNA indicating generation of viroid complementary DNA strands by archaeal reverse transcriptase activity. The actinides and porphyrins modulate RNA folding and catalyse its ribozymal action. Digoxin can cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities[18]. Archaeal pyruvate producing histone deacetylase inhibition and porphyrins intercalating with DNA can produce endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the RNA viroidal complementary DNA into the noncoding region of eukaryotic non coding DNA using HERV integrase as has been described for borna and ebola viruses[19]. The archaea and viroids can also induce cellular porphyrin synthesis. Bacterial and viral infections can precipitate metabolic syndrome-type 2 diabetes mellitus, CVA and CAD[20-23].

The porphyrins can undergo photooxidation generating free radicals. The archaeal porphyrins can produce free radical injury. The porphyrins can complex and intercalate with the cell membrane producing sodium potassium ATPase inhibition adding on to digoxin mediated inhibition. Porphyrins can complex with proteins and nucleic acid producing biophoton emission. Porphyrins complexing with proteins can modulate protein structure and function. Porphyrins complexing with DNA and RNA can modulate transcription and translation. The porphyrin especially protoporphyrins can bind to peripheral benzodiazepine receptors in the mitochondria and modulate its function, mitochondrial cholesterol transport and steroidogenesis. Peripheral benzodiazepine receptor modulation by protoporphyrins can regulate cell death, cell proliferation, immunity and neural

functions. The porphyrin photo-oxidation generates free radicals which can modulate enzyme function. Redox stress modulated enzymes include pyruvate dehydrogenase, nitric oxide synthase, cystathione beta synthase and heme oxygenase. Free radicals can modulate mitochondrial PT pore function. Free radicals can modulate cell membrane function and inhibit sodium potassium ATPase activity. Thus the porphyrins are key regulatory molecules modulating all aspects of cell function[20-23]. This can contribute to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

The dipolar porphyrins, PAH and archaeal magnetite in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated Frohlich model superconducting state[22] inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world[4, 22]. Porphyrins binding to proteins, nucleic acids and cell membranes can produce biophoton emission. Biophotons can mediate quantal perception. Cellular porphyrins photo-oxidation are involved in sensing of earth magnetic fields and low level biomagnetic fields. Thus prophyrins can mediate extrasensory perception of low level EMF contributing to metabolic syndrome x, CVA and CAD. Porphyrin induced increased NMDA transmission and free radical injury can contribute to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Free radicals can produce mitochondrial PT pore dysfunction. This can lead to cyto C leak and activation of the caspase cascade leading to apoptosis and cell death. Altered porphyrin metabolism has been described in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The protoporphyrins binding to mitochondrial benzodiazepine receptors can regulate brain function[20-23]. This can lead to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

The porphyrin photo-oxidation can generate free radicals which can activate NFKB. This can produce immune activation and cytokine mediated injury. The increase in archaeal porphyrins can lead to autoimmunity in metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. The protoporphyrins binding to mitochondrial benzodiazepine receptors can modulate immune function[20-23].

The porphyrin photo-oxidation mediated free radical injury can lead to insulin resistance and atherogenesis. Thus archaeal porphyrins can contribute to metabolic syndrome x. Glucose has got a negative effect upon ALA synthase activity. Therefore hyperglycemia may be reactive protective mechanism to increased archaeal porphyrin synthesis. The protoporphyrins binding to mitochondrial benzodiazepine receptors can modulate mitochondrial steroidogenesis and metabolism. Altered porphyrin metabolism has been described in the metabolic syndrome-type 2 diabetes mellitus with CAD and CVA. Porphyrias can lead onto vascular thrombosis. The porphyrin photo-oxidation can generate free radicals inducing HIF alpha[20-23]. This can lead to the pathogenesis of type 2 diabetes mellitus with CAD and CVA.

The porphyrin can combine with prion proteins modulating their conformation. This leads to abnormal prion protein conformation and degradation. Archaeal porphyrins can contribute to prion disease. The porphyrins can intercalate with DNA producing HERV expression. The HERV particles generated can contribute to the retroviral state[20-23]. HERV sequences and prion protein are related to metabolic syndrome-type 2 diabetes mellitus, CVA and CAD.

Thus the archaeal porphyrins can contribute to the pathogenesis of metabolic syndrome-type 2 diabetes mellitus, CVA and CAD. Archaeal porphyrin synthesis is crucial in the pathogenesis of these disorders. Porphyrins may serve as regulatory molecules modulating immune, neural, endocrine, metabolic and genetic systems. The porphyrins photo-oxidation generated free radicals can

produce immune activation and produce insulin resistance. The archaeal porphyrins functions as key regulatory molecules with mitochondrial benzodiazepine receptors playing an important role[20-23].

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