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Endosymbiotic Actinidic Archaea/Viroids, Hemispheric Dominance and the Tridosha Theory

Introduction

The human brain synthesises an endogenous membrane sodium potassium ATPase inhibitor digoxin which plays a role in neuro-immuno-endocrine integration and pathogenesis of several neuropsychiatric and systemic diseases. Endomyocardial fibrosis (EMF) along with the root wilt disease of coconut is endemic to Kerala with its radioactive actinide beach sands. Actinides like rutile producing intracellular magnesium deficiency due to rutile-magnesium exchange sites in the cell membrane have been implicated in the etiology of EMF[1]. Endogenous digoxin, a steroidal glycoside which functions as a membrane sodium-potassium ATPase inhibitor has also been related to its etiology due to the intracellular magnesium deficiency it produces.[2] Organisms like phytoplasmas and viroids have also been demonstrated to play a role in the etiology of these diseases.[3, 4] Endogenous digoxin has been related to hemispheric dominance.[2] Right hemispheric dominant individuals were hyperdigoxinemic, left hemispheric dominant individuals were hypodigoxinemic and bihemispheric dominant individuals were normodigoxinemic. The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered.[5, 6, 7] An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described.[6] The intracellular endosymbionts archaea and their intron derived viroids constitute the third element regulating the human body.

Ayurveda, the traditional Indian System of Medicine, deals with the theory of the three tridosha states (both physical and psychological): Vata, Pitta and Kapha. They are the three major human constitutional types that both depend on psychological and physical characteristics. The Pitta state is described as a

critical, discriminative, and rational psychological state of mind, while the Kapha state is described as being dominant for emotional stimuli. The Vata state is an intermediate unstable shifting state. The Pitta types are of average height and built with well developed musculature. The Vata types are thin individuals with low body mass index. The Kapha types are short stocky individuals that tend toward obesity, and who are sedentary. Previous work in our laboratory had correlated the tridosha states of Kapha, Pitta and Vata with hemispheric dominance and endogenous digoxin status. The Kapha state has been demonstrated as equivalent to right hemispheric dominant hyperdigoxinemic state. The Pitta state has been demonstrated as equivalent to the left hemispheric dominant hypodigoxinemic state. The Vata state has been demonstrated as equivalent to the bihemispheric dominant normodigoxinemic state.[8] The study assessed actinidic archaea and viroids in the tridosha states of Ayurveda. The results are presented in this paper.

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: - (I) right handed-left hemispheric dominant-pitta group, (II) left handed-right hemispheric dominant-kapha group and (III) amphidextrous-bihemispheric dominant-vata group of individuals. Hemispheric dominance was assessed by methods described in previous reports.[2] There were 10 healthy normal individuals in the age range between 20 to 30 years in each group. They were selected randomly from the general population. The blood samples were drawn in the fasting state. 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.[9] 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, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, dopamine, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids.[10, 11, 12, 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. The statistical analysis was done by ANOVA.

Results

The parameters checked as indicated above were: - cytochrome F420, free RNA, free DNA, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids. The plasma of the bihemispheric dominant group showed detectable levels of the above mentioned parameters after incubation for 1 hour and addition of cholesterol substrate resulted in still further increase in these parameters. The addition of antibiotics to the *bihemispheric dominant vata group* caused a decrease in all the parameters while addition of rutile increased their levels. The plasma of *right hemispheric dominant kapha group* showed a significant increase in the above mentioned parameters as compared to *bihemispheric dominant vata group*. The addition of antibiotics to the *right hemispheric dominant kapha group* caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in *right hemispheric dominant kapha group* as compared to *bihemispheric dominant vata group*. The plasma of *left hemispheric dominant pitta group* showed a

significant decrease in the above mentioned parameters as compared to the *bihemispheric dominant vata group*. The addition of antibiotics to the *left hemispheric dominant pitta group* caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was less in *left hemispheric dominant pitta group* as compared to *bihemispheric dominant vata group*. 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 cytochorme F420 and muramic acid.*

Group	CYT F420% change (Increase with Rutile)		CYT F420% change (Decrease with antibiotics)		Muramic acid % change (Increase with Rutile)		Muramic acid % change (Decrease with antibiotics)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
BHD/VATA	4.48	0.15	18.24	0.66	4.34	0.15	18.24	0.37
RHD/KAPHA	11.35	0.64	60.49	6.22	22.68	1.99	63.29	5.93
LHD/PITTA	2.13	0.13	5.37	1.47	2.26	0.25	7.45	0.40
F value	306.749		130.054		348.867		364.999	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with antibiotics)		RNA % change (Increase with Rutile)		RNA % change (Decrease with antibiotics)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
BHD/VATA	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
RHD/KAPHA	22.99	1.56	65.19	4.10	23.27	1.36	65.66	3.93
LHD/PITTA	2.26	0.25	7.45	0.40	2.30	0.12	7.62	0.30
F value	337.577		356.621		427.828		654.453	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	HMG CoA R % change (Increase with Rutile)		HMG CoA R % change (Decrease with antibiotics)		PAH % change (Increase with Rutile)		PAH % change (Decrease with antibiotics)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
BHD/VATA	4.30	0.20	18.35	0.35	4.45	0.14	18.25	0.72
RHD/KAPHA	21.06	2.32	63.87	6.22	21.00	2.54	57.42	7.07
LHD/PITTA	2.33	0.17	7.24	0.59	2.25	0.17	7.01	0.65
F value	319.332		199.553		391.318		257.996	
P value	< 0.001		< 0.001		< 0.001		< 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 antibiotics)		Bile Acids % change (Increase with Rutile)		Bile Acids % change (Decrease with antibiotics)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
BHD/VATA	0.11	0.00	0.054	0.003	4.29	0.18	18.15	0.58
RHD/KAPHA	0.55	0.10	0.248	0.058	21.10	2.43	54.82	8.28
LHD/PITTA	0.07	0.01	0.026	0.004	2.25	0.19	7.25	0.66
F value	135.116		71.706		290.441		203.651	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with antibiotics)		Hexokinase % change (Increase with Rutile)		Hexokinase % change (Decrease with antibiotics)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
BHD/VATA	4.34	0.21	18.43	0.82	4.21	0.16	18.56	0.76
RHD/KAPHA	11.12	0.66	59.68	6.24	23.27	1.68	67.35	3.77
LHD/PITTA	2.16	0.18	5.91	1.38	2.24	0.17	6.29	1.06
F value	321.255		115.242		292.065		317.966	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	ATP synthase % change (Increase with Rutile)		ATP synthase % change (Decrease with antibiotics)		H_2O_2 % change (Increase with Rutile)		H_2O_2 % change (Decrease with antibiotics)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
BHD/VATA	4.40	0.11	18.78	0.11	4.43	0.19	18.13	0.63
RHD/KAPHA	11.99	0.38	66.34	3.39	17.60	3.53	54.68	5.09
LHD/PITTA	2.30	0.12	7.62	0.30	2.24	0.23	5.36	0.99
F value	449.503		673.081		380.721		171.228	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 7. *Effect of rutile and antibiotics on delta amino levulinic acid and dopamine.*

Group	ALA % (Increase with Rutile)		ALA % (Decrease with antibiotics)		DOPAMINE % change (Increase with Rutile)		DOPAMINE % change (Decrease with antibiotics)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
BHD/VATA	4.40	0.10	18.48	0.39	4.41	0.15	18.63	0.12
RHD/KAPHA	22.98	2.06	66.10	4.03	11.36	0.58	65.41	4.83
LHD/PITTA	2.13	0.11	7.62	0.32	2.13	0.11	7.62	0.32
F value	372.716		556.411		403.394		680.284	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Abbreviation

BHD: Bihemispheric dominance/vata

RHD: Right hemispheric dominance/kapha

LHD: Left hemispheric dominance/pitta

Discussion

Ayurveda, the traditional Indian System of Medicine, deals with the theory of the three tridosha states (both physical and psychological): Vata, Pitta and Kapha. They are the three major human constitutional types that both depend on

psychological and physical characteristics. The Pitta state is described as a critical, discriminative, and rational psychological state of mind, while the Kapha state is described as being dominant for emotional stimuli. The Vata state is an intermediate unstable shifting state. The Pitta types are of average height and built with well developed musculature. The Vata types are thin individuals with low body mass index. The Kapha types are short stocky individuals that tend toward obesity, and who are sedentary. The study assessed the biochemical differences between right hemispheric dominant, bihemispheric dominant, and left hemispheric dominant individuals, and then compared this with the patterns obtained in the Vata, Pitta, and Kapha states. The isoprenoid metabolites (digoxin, dolichol, and ubiquinone), glycoconjugate metabolism, free radical metabolism, and the RBC membrane composition were studied. The hemispheric chemical dominance in various systemic diseases and psychological states was also investigated. The results showed that right hemispheric chemically dominant/Kapha state had elevated digoxin levels, increased free radical production and reduced scavenging, increased tryptophan catabolites and reduced tyrosine catabolites, increased glycoconjugate levels and increased cholesterol: phospholipid ratio of RBC membranes. Left hemispheric chemically dominant/Pitta states had the opposite biochemical patterns. The patterns were normal or intermediate in the bihemispheric chemically dominant/Vata state. This pattern could be correlated with various systemic and neuropsychiatric diseases and personality traits. Right hemispheric chemical dominance/Kapha state represents a hyperdigoxinemic state with membrane sodium-potassium ATPase inhibition. Left hemispheric chemical dominance/Pitta state represents the reverse pattern with hypodigoxinemia and membrane sodium-potassium ATPase stimulation. The Vata state is the intermediate bihemispheric chemical dominant state. Ninety-five percent of the patients/individuals in the tridosha, pathological, and psychological groups were right-handed/left hemispheric dominant, however,

their biochemical patterns were different-either left hemispheric chemical dominant or right hemispheric chemical dominant. Hemispheric chemical dominance/tridosha states had no correlation with cerebral dominance detected by handedness/dichotic listening test.[8]

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesise and use cholesterol as a carbon and energy source.[14, 15] 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.[16] 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.[7] The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide.[15] 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.[17] 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.[18] 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.[19] The decrease in free self replicating RNA and DNA with the addition of antibiotics indicates that the RNA viroids are derived from archaeal

introns. 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.[20] 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[21]. The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites.[20, 21] This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters.[22] The viroidal complementary DNA can function as jumping genes producing a dynamic genome important in storage of synaptic information, HLA gene expression and neurodevelopmental gene expression. The alteration in DNA sequences produced by viroidal complementary DNA jumping genes can lead onto schizophrenia and primary seizure disorder. The RNA viroids can regulate mRNA function by RNA interference.[19] The phenomena of RNA interference can modulate T cell and B cell function, neuronal transmission and euchromatin/heterochromatin expression. The RNA viroid induced mRNA interference can modulate dopaminergic, glutamatergic and serotoninergic synaptic transmission. The archaea and viroidal density is high in right hemispheric dominant kapha group, intermediate in bihemispheric dominant vata group and low in left hemispheric dominant pitta group.

The presence of muramic acid, HMG CoA reductase and cholesterol oxidase activity inhibited by antibiotics indicates the presence of bacteria with mevalonate pathway. The density of the mevalonate pathway bacterial is high in right hemispheric dominant kapha state, low in left hemispheric dominant pitta state and intermediate in bihemispheric dominant vata state. The bacterial with mevalonate pathway include streptococcus, staphylococcus, actinomycetes, listeria, coxiella

and borrelia.[23] The bacteria and archaea with mevalonate pathway and cholesterol catabolism had a evolutionarily advantage and constitutes the isoprenoidal clade organism with the archaea evolving into mevalonate pathway gram positive and gram negative organism through horizontal gene transfer of viroidal and virus genes.[24] The isoprenoidal clade prokaryotes develop into other groups of prokaryotes via viroidal/virus as well as eukaryotic horizontal gene transfer producing bacterial speciation.[25] 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 eukaryotic and human genes resulting in viral speciation. Bacterial and 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 prokaryotic and viral speciation. The multicellular eukaryote developed so that their endosymbiotic archaeal colonies could survive and forage better. The multicellular eukaryotes are like bacterial biofilms. The archaea and bacteria with a mevalonate pathway uses the extracellular RNA viroids and DNA viroids for quorum sensing and in the generation of symbiotic biofilm like structures which develop into multicellular eukaryotes.[26, 27] The endosymbiotic archaea and bacteria with mevalonate pathway still uses the RNA viroids and DNA viroids for the regulation of muticellular eukaryote. Pollution is induced by the primitive nanoarchaea and mevalonate pathway bacteria synthesised 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.[28] 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. Bacteria and viruses can contribute to the regulation of hemispheric dominance and tridoshas as exemplified by schizophrenia, a disorder of consciousness. Borrelia, toxoplasma, chlamydia, mycoplasma, retroviruses, herpes virus, influenza virus and borna virus contribute to the neuropathogenesis of schizophrenia.[29, 30, 31] The change in the length and grammar of the noncoding region produces eukaryotic speciation and individuality.[32] Changes in the length of noncoding region can lead onto modulation of hemispheric dominance/tridoshas and conscious perception as exemplified in schizophrenia.[33] The human endogenous retroviruses and change in the length and grammar of the noncoding region has been described in schizophrenia. 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 producing microchimeras. Microchimeras can also generate tissue and neuronal polyploidy. The higher degree of integration of archaea, mevalonate pathway bacteria and viroids into the genome produces right hemispheric dominant kapha group, intermediate degree of integration produces bihemispheric dominant vata group and lower degree of integration left hemispheric dominant pitta group.

The archaea and viroids can regulate the nervous system including the NMDA/GABA thalamo-cortico-thalamic pathway mediating conscious

perception.[2, 34] NMDA/GABA receptors can be modulated by digoxin induced calcium oscillations resulting in NMDA/glutamic acid decarboxylase (GAD) activity induction, PAH increasing NMDA activity and inducing GAD as well as viroid induced RNA interference modulating NMDA/GABA receptors.[2] The cholesterol ring oxidase generated pyruvate can be converted by the GABA shunt pathway to glutamate and GABA. Increased NMDA transmission has been described in schizophrenia and primary seizure disorder. The dipolar 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.[2, 34] The archaea can regulate limbic lobe transmission with archaeal cholesterol aromatase/ring oxidase generated norepinephrine, dopamine, serotonin and acetyl choline.[17] Thus the shadow biosphere of archaea and viroids can regulate conscious and quantal perception. The archaea and viriods can also modulate multiple neurotransmitter systems. Schizophrenia is described as a disorder of consciousness and increased integration of archaea and viroids into the genome can contribute to its neuropathogenesis. Increased dopaminergic, serotoninergic and NMDA transmission is important in the pathogenesis of schizophrenia. The higher degree of integration of the archaea into the genome produces increased digoxin synthesis producing right hemispheric dominant kapha group and lesser degree producing left hemispheric dominant pitta group.[2] Bihemispheric dominant vata group is intermediate with normal digoxin synthesis. Right hemispheric dominant kapha group has been described in schizophrenia. The increased integration of archaea into the neuronal genome can produce increased cholesterol oxidase and aromatase mediated monoamine and NMDA transmission producing schizophrenia. The archaeal bile acids are chemically diverse and structurally different from human bile acids. The archaeal

bile acids can bind olfactory GPCR receptors and stimulate the limbic lobe producing a sense of social identity. The dominance of archaeal bile acids over human bile acids in stimulating the olfactory GPCR-limbic lobe pathway leads to loss of social identity leading to schizophrenia and autism.[35]

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 signalling can activate NFKB producing chronic immune activation.[2, 36] The archaea and viroid induced chronic immune activation and generation of superantigens can lead on to autoimmune disease. This produces a state of chronic immune activation in right hemispheric dominant kapha group producing increased predisposition to autoimmune diseases. The left hemispheric dominant pitta group is immunosuppressed and the bihemispheric dominant vata group has normal immune function.

Archaea, viroids and digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype.[37] 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. The immune activation mediated increased levels of TNF alpha can produce insulin resistance acting at the level of insulin receptor. Thus a state similar to metabolic syndrome X exists in right hemispheric dominant kapha group. Left hemispheric dominant pitta group can have a pattern of increased insulin sensitivity and low body mass index producing a reverse metabolic syndrome x. The bihemispheric dominant vata state will be metabolically intermediate. Cholesterol oxidase activity, increased glycolysis related NADPH oxidase activity and mitochondrial

dysfunction generates free radicals. Free radical production and mitochondrial dysfunction can increase NMDA transmission important in conscious perception. 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.[37] The increased cholesterol substrate leads to increased archaeal growth and digoxin synthesis leading to metabolic channelling to the mevalonate pathway. Hyperdigoxinemia is important in the regulation of hemispheric dominance and the tridoshas.[2] The right hemispheric dominant kapha group is hyperdigoxinemic, left hemispheric dominant pitta group is hypodigoxinemic and bihemispheric dominant vata group is normodigoxinemic. The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy needs. Ammonia can regulate both NMDA and GABA transmission depending on its levels.

The Warburg phenotype can contribute to the hemispheric dominance and tridoshas by augmenting the bacterial shikimic acid pathway. The upregulated glycolysis consequent to the Warburg phenotype produces phosphoenolpyruvate, a basic substrate for the bacterial shikimic acid pathway which can synthesise monoamines and neuroactive alkaloids. The shikimic acid pathway can generate dopamine and serotonin producing increased monoaminergic transmission. The shikimic acid pathway can also synthesise the neuroactive alkaloids strychnine, nicotine, morphine, mescaline and LSD important in regulating neural transmission.[2] The upregulated glycolysis can also contribute to increased NMDA and GABA transmission in the thalamo-cortico-thalamic pathway. The glycolytic pathway produces phosphoglycerate which is converted to phosphoserine and then serine which activates the NMDA receptor. The glycolytic enzyme glyceraldehyde-3-phosphate dehydrogenase is a GABA receptor kinase and activates GABA transmission. Thus the archaea and viroid induced Warburg phenotype can contribute to the modulation of hemispheric dominance and

tridoshas by regulating the multiple neurotransmitter systems. The archaeal cholesterol catabolism can deplete the cell membranes of cholesterol resulting in alteration in lipid microdomains and their related neurotransmitter receptor contributing to the regulation of NMDA, serotoninergic and dopaminergic transmission. Thus the archaeal cholesterol catabolism and viroids can regulate brain function and hemispheric dominance/tridoshas. The archaea and viroids have axonal and transynaptic transport functioning as biological neurotransmitters. The brain can be visualized evolutionarily as a modified mevalonate pathway bacteria and archaeal colony functioning by mechanisms of quorum sensing using RNA viroids with its bacterial flagellar system forming axo-axonic and axo-dendritic connections. The third element of archaea and their derived viroids can also regulate the immune, genetic, metabolic and neural systems producing its integration.

The third element formed of intracellular archaea and viroidal symbiosis determines hemispheric dominance and tridoshas. Also archaeal cholesterol synthesis and cholesterol catabolism determines hemispheric dominance and tridoshas.

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2

A Cholesterol and Actinide Dependent Shadow Biosphere of Archaea and Viroids

Introduction

Endomyocardial fibrosis along with the root wilt disease of coconut is endemic to Kerala with its radioactive actinide beach sands. Actinides like rutile, endogenous digoxin as well as organisms like phytoplasmas and viroids have been implicated in the etiology of these diseases.[1-4] Endogenous digoxin has been related to the pathogenesis of schizophrenia, malignancy, metabolic syndrome x, autoimmune disease and neuronal degeneration.[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 the above mentioned disease states 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 synthesised 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:- endomyocardial fibrosis, Alzheimer's disease, multiple sclerosis, non-hodgkin's lymphoma, metabolic syndrome x with cerebrovascular thrombosis and coronary artery disease, schizophrenia, autism, seizure disorder, Creutzfeldt Jakob disease and acquired immunodeficiency syndrome. 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 redutase, 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
Schizo	23.24	2.01	58.72	7.08	23.01	1.69	59.49	4.30
Seizure	23.46	1.87	59.27	8.86	22.67	2.29	57.69	5.29
AD	23.12	2.00	56.90	6.94	23.26	1.53	60.91	7.59
MS	22.12	1.81	61.33	9.82	22.83	1.78	59.84	7.62
NHL	22.79	2.13	55.90	7.29	22.84	1.42	66.07	3.78
DM	22.59	1.86	57.05	8.45	23.40	1.55	65.77	5.27
AIDS	22.29	1.66	59.02	7.50	23.23	1.97	65.89	5.05
CJD	22.06	1.61	57.81	6.04	23.46	1.91	61.56	4.61
Autism	21.68	1.90	57.93	9.64	22.61	1.42	64.48	6.90
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
Schizo	23.28	1.70	61.41	3.36	23.59	1.83	65.69	3.94
Seizure	23.40	1.51	63.68	4.66	23.08	1.87	65.09	3.48
AD	23.52	1.65	64.15	4.60	23.29	1.92	65.39	3.95
MS	22.62	1.38	63.82	5.53	23.29	1.98	67.46	3.96
NHL	22.42	1.99	61.14	3.47	23.78	1.20	66.90	4.10
DM	23.01	1.67	65.35	3.56	23.33	1.86	66.46	3.65
AIDS	22.56	2.46	62.70	4.53	23.32	1.74	65.67	4.16
CJD	23.30	1.42	65.07	4.95	23.11	1.52	66.68	3.97
Autism	22.12	2.44	63.69	5.14	23.33	1.35	66.83	3.27
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 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
Schizo	22.91	1.92	61.63	6.79	23.67	1.42	67.39	3.13
Seizure	23.09	1.69	61.62	8.69	23.09	1.90	66.15	4.09
AD	23.43	1.68	61.68	8.32	23.58	2.08	66.21	3.69
MS	23.14	1.85	59.76	4.82	23.52	1.76	67.05	3.00
NHL	22.28	1.76	61.88	6.21	24.01	1.17	66.66	3.84
DM	23.06	1.65	62.25	6.24	23.72	1.73	66.25	3.69
AIDS	22.86	2.58	66.53	5.59	23.15	1.62	66.48	4.17
CJD	22.38	2.38	60.65	5.27	23.00	1.64	66.67	4.21
Autism	22.72	1.89	64.51	5.73	22.60	1.64	66.86	4.21
EMF	22.92	1.48	61.91	7.56	23.37	1.31	63.97	3.62
	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
Schizo	0.55	0.06	0.219	0.043	23.20	1.87	57.04	4.27
Seizure	0.51	0.05	0.199	0.027	22.61	2.22	66.62	4.99
AD	0.55	0.03	0.192	0.040	22.12	2.19	62.86	6.28
MS	0.52	0.03	0.214	0.032	21.95	2.11	65.46	5.79
NHL	0.54	0.04	0.210	0.042	22.98	2.19	64.96	5.64
DM	0.47	0.04	0.202	0.025	22.87	2.58	64.51	5.93
AIDS	0.56	0.05	0.220	0.052	22.29	1.47	64.35	5.58
CJD	0.53	0.06	0.212	0.045	23.30	1.88	62.49	7.26
Autism	0.53	0.08	0.205	0.041	22.21	2.04	63.84	6.16
EMF	0.51	0.05	0.213	0.033	23.41	1.41	58.70	7.34
	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
Schizo	20.99	1.46	61.23	9.73	23.01	2.61	65.87	5.27
Seizure	20.94	1.54	62.76	8.52	23.33	1.79	62.50	5.56
AD	22.63	0.88	56.40	8.59	22.96	2.12	65.11	5.91
MS	21.59	1.23	60.28	9.22	22.81	1.91	63.47	5.81
NHL	21.19	1.61	58.57	7.47	22.53	2.41	64.29	5.44
DM	20.67	1.38	58.75	8.12	23.23	1.88	65.11	5.14
AIDS	21.21	2.36	58.73	8.10	21.11	2.25	64.20	5.38
CJD	21.07	1.79	63.90	7.13	22.47	2.17	65.97	4.62
Autism	21.91	1.71	58.45	6.66	22.88	1.87	65.45	5.08
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 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
Schizo	22.50	1.66	60.21	7.42	22.52	1.90	66.39	4.20
Seizure	23.81	1.19	61.08	7.38	22.83	1.90	67.23	3.45
AD	22.65	2.48	60.19	6.98	23.67	1.68	66.50	3.58
MS	21.14	1.20	60.53	4.70	22.38	1.79	67.10	3.82
NHL	23.35	1.76	59.17	3.33	23.34	1.75	66.80	3.43
DM	23.27	1.53	58.91	6.09	22.87	1.84	66.31	3.68
AIDS	23.32	1.71	63.15	7.62	23.45	1.79	66.32	3.63
CJD	22.86	1.91	63.66	6.88	23.17	1.88	68.53	2.65
Autism	23.52	1.49	63.24	7.36	23.20	1.57	66.65	4.26
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	

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
Schizo	21.88	1.19	66.28	3.60	23.02	1.65	67.61	2.77
Seizure	22.29	1.33	65.38	3.62	22.13	2.14	66.26	3.93
AD	23.66	1.67	65.97	3.36	23.09	1.81	65.86	4.27
MS	22.92	2.14	67.54	3.65	21.93	2.29	63.70	5.63
NHL	23.81	1.90	66.95	3.67	23.12	1.71	65.12	5.58
DM	24.10	1.61	65.78	4.43	22.73	2.46	65.87	4.35
AIDS	23.43	1.57	66.30	3.57	22.98	1.50	65.13	4.87
CJD	23.70	1.75	68.06	3.52	23.81	1.49	64.89	6.01
Autism	22.76	2.20	67.63	3.52	22.79	2.20	64.26	6.02
EMF	22.28	1.52	64.05	2.79	22.82	1.56	64.61	4.95
	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 synthesise 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 signalling

lipid metabolism, cell growth and differentiation, apoptosis, neuronal transmission and euchromatin / heterochromatin expression.

The archaea and viroids can regulate the nervous system including the NMDA/GABA thalamo-cortico-thalamic pathway mediating conscious perception.[4, 22] NMDA/GABA receptors can be modulated by digoxin induced calcium oscillations resulting NMDA/GAD activity induction, PAH increasing NMDA activity and inducing GAD as well as viroid induced RNA interference.[4] The cholesterol ring oxidase generated pyruvate can be converted by the GABA shunt pathway to glutamate and GABA. The dipolar 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] The archaea can regulate limbic lobe transmission with archaeal cholesterol aromatase/ring oxidase generated norepinephrine, dopamine, serotonin and acetyl choline.[16] The higher degree of integration of the archaea into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance.[4] The increased integration of archaea into the neuronal genome can produce increased cholesterol oxidase and aromatase mediated monoamine and NMDA transmission producing schizophrenia and autism. 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 signalling 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 autoimmune disease. 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 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.[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 channelling 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 Warburg phenotype induced increased mitochondrial PT pore hexokinase, archaeal PAH and viroid induced RNA interference can lead on to malignant transformation. The digoxin and PAH induced increased intracellular calcium can lead to PT pore dysfunction, cell death and neuronal degeneration.[4] The archaeal cholesterol catabolism can deplete the cell membranes of cholesterol resulting in organelle dysfunction and degeneration. 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. The archaeal digoxin and rutile induced magnesium depletion can lead MPS deposition and produce EMF, CCP, MNG and mucoid angiopathy.[4]

The metal actinides provide radiolytic energy, catalysis for oligomer formation and provide a coordinating ion for metalloenzymes all important in abiogenesis.[7] The metal actinide surfaces would by surface metabolism generate acetate which could get converted to acetyl CoA and then to cholesterol which functions as the primal prebiotic molecule self organizing into self replicating supramolecular systems, the lipid organism.[9, 26, 27] Cholesterol by radiolysis by actinides would have formed PAH generating PAH aromatic organism.[9] Cholesterol radiolysis would generate pyruvate which would get converted to amino acids, sugars, nucleotides, porphyrins, fatty acids and TCA acids. Anastase and rutile surfaces can produce polymerization of amino acids, isoprenyl residues, PAH and nucleotides to generate the initial lipid organism, PAH organism, prions and RNA viroids which would have symbiosed to generate the archaeal protocell. The archaea evolved into gram negative and gram positive bacteria with a mevalonate pathway which had a evolutionary advantage and the symbiosis of archaea with gram negative organism generated the eukaryotic cell.[28] The data supports the persistence of an actinide and cholesterol based shadow biosphere which throws light on the actinide based origin of life and cholesterol as the premier prebiotic molecule.

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3

The Archaeal Induced Stem Cell Conversion Produces an Epidemic Benjamin Buttons Reverse Aging Syndrome Leading to Cancer and a Spiritual, Surrealistic Evil Brain

Open Science

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 cancer. In all these systemic diseases 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.[1-17]

The idea of goodness is based on reason and logic. Reason judgment and logic is a function of the cerebral cortex especially the prefrontal lobe. Prefrontal lobe function needs dynamic synaptic connectivity which is produced by jumping genes mediated by human endogenous retroviral sequences. Goodness is correlated with heaven. The idea of evil is based on the unconscious and the impulsive behaviour related to subcortical areas especially the cerebellum. The cerebellum is the site of impulsive behaviour and the unconscious behaviour. The cerebellar and subcortical brain connections are predominantly archaeal colony networks. The idea of evil is related to hell. The idea of conscious judgmental acts and unconscious impulsive acts, heaven and hell, goodness and evil are

juxtapositions. 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 systemic diseases, neuropsychiatric disorders and normal individuals with differing psychological profile-prisoners, creative individuals and common sense modulated business men.[1-17] The results are presented in this paper.

Materials and Methods

The blood samples were drawn from four groups of psychological different population spiritually inclined, criminal prisoners, creative artists and business men. There were 15 members in each group. The blood samples were also drawn from 15 cases each brain glioma, NHL and people exposed to low level irradiation. 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 results showed that the spiritual, artistic creative individuals and criminal prisoners had increased cytochrome F420 activity and RBC digoxin levels. The results showed that the businessmen had decreased cytochrome F420 activity and RBC digoxin levels. The blood samples of cancer-brain glioma 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 disease state 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 disease group and in creative artists and criminals suggesting stem cell conversion. This suggests that artistic creative, criminal prisoners as well as spiritual individuals 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
Spiritual	4.00	0.00	12.39	1.23	25.99	8.10	100.51	12.32	5.46	2.83
Acquisitive capitalist	0.00	0.00	1.21	0.38	2.75	0.41	23.79	2.51	0.68	0.23
Artistic	4.00	0.00	12.84	0.74	23.64	1.43	96.19	12.15	10.12	1.75
Criminality	4.00	0.00	12.72	0.92	25.35	5.52	103.32	13.04	9.44	3.40
NHL	4.00	0.00	11.91	0.49	22.83	1.24	95.81	12.18	7.41	4.22
Glioma	4.00	0.00	13.00	0.42	22.20	0.85	96.58	8.75	7.82	3.51
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
Spiritual	2.51	0.36	3.19	0.32	93.43	4.85	1.41	0.23	55.17	5.85
Acquisitive capitalist	16.49	0.89	0.16	0.02	23.92	3.38	0.18	0.05	8.70	0.90
Artistic	2.51	0.42	3.11	0.36	92.40	4.34	1.40	0.32	46.37	4.87
Criminality	2.19	0.19	3.27	0.39	95.37	5.76	1.51	0.29	47.47	4.34
NHL	2.30	0.26	3.48	0.46	91.62	3.24	1.26	0.23	51.08	5.24
Glioma	2.34	0.43	3.28	0.39	93.20	4.46	1.27	0.24	51.57	2.66
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 cancer syndromes and neuropsychological profiles 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 systemic disease and neuropsychiatric disorders. 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 cancer 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 behaviour. The difference between reality and dreams is lost. The brain is ruled by the senses and impulses. The brain

becomes dysfunctional with more of violent, aggressive and cannibalistic behaviour. The art becomes more abstract and related to the unconscious. 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. This produces more of ritualized behaviour, violent and aggressive tendencies, terrorism, war, sexual obscenities and alternate sexuality. It is a world of the senses. It is also intensely evil as well as spiritual. The inhibition of the conscious due to loss of cortical functions and the dominance of the unconscious leads to mystical experience. There is a overflowing of spirituality. The paradoxical side of this behaviour also dominates. The violence, aggression, obsessive sexuality, magic realism in literature, abstract painting, rock music and dance and modern poetry as well as literature produces transcendence of a different kind. This results in surrealism and syntheism. The loss of function of the neurons results in abnormal psychological profile. 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 lymphocytic stem cells have uncontrolled proliferation and results in NHL. The stem cell proliferation results in oncogenesis. The stem cell metabolonomics with inhibited mitochondrial function and anaerobic glycolysis results in Warburg phenotype. The cancer cell behaves like the stem cell.[1-17]

In the metaphysics of evil the unconscious dominates and the behaviour is impulsive dictated by primitive thoughts. The unconscious modulated by the cerebellum is responsible for automatic acts producing what is called as psychic automatism. The unconscious parallels what Jung described as the archetypes of the collective unconscious. The metaphysics of evil leads to a syntheistic brain with the dominance of the willpower. The primitive archetypes produce concepts

of abstract painting, psychedelic music and dance and postmodern literature or magical realism. All these are modes of connecting with the unconscious. The unconscious produces primitive selfish tendencies leading to individualism and capitalism. The unconscious helps to transcend taboos and creates the surrealistic world. The collective unconscious also produces a sense of spirituality and oneness. It is an impulsive brain with fixations and primitive obsessions. There is cerebellar psychic automatism. This leads to ritualized behaviours. The dominance of the collective unconscious results in ritualized behaviours characteristic of religious worship. The collective unconscious also leads to the creation of obscene art and literature as well as violence which is a form of transcendence. Coprolalic religious ritual ceremonies had been described in some parts of the world. Terrorism and acts of violence are also a type of transcendence. The same phenomena occur in ritual sacrifices in religion, the violence of war and the acquisitiveness of capitalism. The primitive unconscious leads to the will to power. This produces greedy capitalism, dictatorship and fascism. The will to power results in worship of the powerful. It is an individualistic, anarchic, selfish world. The cerebellar world is the primitive world of archetypes in the collective unconscious. The abstract paintings have links with the collective unconscious. The rock music or modern music contains rhythmic primitive chaotic sounds coming out the collective unconscious. The primitive collective unconscious links up post modern literature or magic realism with violence, love, hate, evil, obscenities and death. Thus literature, music, dance and painting helps to overcome reality and rationality producing transcendence. The unconscious brain is formed of an archaeal colony network and is adynamic and inflexible. The loss of function of neurons leads to increased extrasensory perception via archaeal magnetite. This can lead to the lack of development of speech and ritualized behaviours of autism. This also produces the thought disorder, hallucinations and delusions. It looks like an epidemic cerebellar cognitive, affective disorder.[1-17]

The goodness is related to conscious brain localized in the cortical areas. The cortical areas mediate moralistic, functionally atheistic, civil society behaviour. The civil society depends upon common good. The cortical world is a world of morality, rationality, altruism, civility and decencies. This needs inhibitory power of the cerebral cortex. Such a society is non-capitalistic and works for the common good. It tends to be non creative. The primitive collective spirituality and oneness is lost. It is replaced by goodness based on judgment, reasoning and morality. It is a moralistic world where taboos are banned. This 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 comparatively is impulsive, criminal, violent, terroristic with love of war, selfish, acquisitive, spiritual, autistic, obsessive, schizophrenic, obscene, evil, ritualized, artistic, illogical and cruel. It 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 civilizational disease like malignancy. 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 generalised 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 of cancer. 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 also results in societal changes where evil and spirituality dominates. The world of the logical civil society of the Christian world comes to end and paganistic behaviour takes over. The society becomes selfish and dominated by impulsive consumerism and acquisitive capitalism. The world becomes cruel, violent, aggressive and terroristic. Art becomes chaotic and abstract in line with the senses and unconscious. There is a predominance of obsessive and alternate sexuality. Criminal behaviour and cruelty dominates. The world is impulsive psychopathic, creative autistic with features of idiotic savants, ritualistic, chaotic, sexual, ugly, anarchic, violent, evil,

paganistic, obscene, atheistically spiritual as well as selfish. It mimics the Niezteschean world, the deconstructed world of Derrida, the surrealistic world of Bataille and the nihilistic, anarchic world. There is the death of the individual and life becomes a social value. It is an acephalistic world of Freud and Jung. The art is abstract, the literature is magically real, the music is rock and the dance chaotic. All these results from the extinction of rationality and the dominance of primitive impulsive behaviour. A civilization of the senses dominated by the unconscious takes over. The will to goodness given by the cerebral cortex is lost. This results in development of a new homo neoneanderthal human species with its dominant evilly spiritual cerebellar brain. It produces a surrealistic evil brain with realm of the senses, archetypes, evil spirituality and impulsiveness taking over. It is a kingdom of the collective unconscious and selfish capitalism with the will to power and the realm of the senses and cancer.[1-17]

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4

Neanderthal Hybrids: Climate Change Mediated Actinidic Archaeal Endosymbiosis Generates Neanderthal Hybrids and Mind-Body Phenotypic Change – The Origins of Schizophrenia, Autism and Epilepsy

Introduction

Actinidic archaea has been related to global warming and human diseases especially schizophrenia, autism and epilepsy. 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 schizophrenia, autism and epilepsy especially the Warburg phenotype and hyperdigoxinemia. Digoxin produced by archaeal cholesterol catabolism produces Neanderthalisation. Prefrontal cortical atrophy and cerebellar hyperplasia has been related to schizophrenia, autism and epilepsy 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.[1-16] The data is described in this paper.

Materials and Methods

Fifteen cases, each of schizophrenia, autism and epilepsy and 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
Schizophrenia	69%	75%	65%
Autism	80%	75%	72%
Epilepsy	80%	75%	75%
Internet users	65%	72%	69%

Table 2. *Neanderthal phenotype and brain dysfunction.*

Disease	Dysautonomia	Prefrontal cortex atrophy	Cerebellar hypertrophy
Schizophrenia	65%	60%	70%
Autism	72%	69%	72%
Epilepsy	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.

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. 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.

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 schizophrenia and autism. There is an epidemic of autism and schizophrenia in the present day community. The porphyrin mediated extrasensory perception can contribute to communication among Neanderthals. Neanderthals did not have a language and used extrasensory perception as a form of group communication. Because of dominant extrasensory quantal perception, the Neanderthals did not have individual identity but only group identity. Cerebellar dominance results in creativity consequent to quantal perception and group perception. The neanderthalic traits contribute to innovation and creativity. Cerebellar dominance results in development of a symbolic language. The Neanderthals used dance and music as a form of communication. Painting as a form of communication was also common in Neanderthals. Neanderthal behaviour was robotic. Robotic behaviour is characteristic of cerebellar dominance. Robotic, symbolic and ritualistic behaviour is common with cerebellar dominance and is seen in autistic traits. The cerebellar dominance in

Neanderthals leads to intuitive intelligence and a hypnotic quality to communication. The increased extrasensory quantal perception leads to more communion with nature and a form of eco-spirituality. The increasing use of dance and music as a form of communication and eco-spirituality is common in the modern century along with increased incidence of autism. The cholesterol depletion leads to bile acid deficiency and generation of small social groups in Neanderthals. Bile acid binds to olfactory receptors and contributes to group identity. This can also contributes to the generation of autistic and schizophrenic features in Neanderthals. This also contributes to epileptogenesis.

The Neanderthal population was predominantly autistic and schizophrenic. The modern population is a hybrid of homo sapiens and homo neanderthalis. This contributes to 10 to 20 per cent dominant hybrids who tend to have schizophrenic and autistic qualities and contributes to creativity of civilisation. The Neanderthals tend to be innovative and chaotic. They tend to be creative in art, literature, dance, spirituality and science. Eighty per cent of less dominant hybrids are stable and contribute to a stabilizing influence leading to growth of civilisation. The homo sapiens were stable and non-creative over a long period of their existence. There was a burst of creativity with generation of music, dance, painting, ornaments, the creation of concept of God and compassionate group behaviour around 10,000 years ago in the homo sapiens community. This correlated with the generation of Neanderthal hybrids when the Eurasian Neanderthal male mated with homo sapiens African females. The extrasensory/quantal perception due to dipolar porphyrins and digoxin induced sodium potassium ATPase inhibition and the generated pumped phonon system mediated quantal perception leads to the globalisation phenomena and feeling of the world being a global village. The archaeal cholesterol catabolism leads to increased synthesis of digoxin. 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 addiction traits and creativity. The increased tryptophan levels produce increased alkaloids like LSD contributing to ecstasy and spirituality of Neanderthal population. Addictive, ADHD and autistic features are related to the morphine deficiency state. The ketogenic diet consumed by the meat eating Neanderthals leads on to increased generation of hydroxy butyric acid which produces ecstasy and a dissociative type of anaesthesia contributing to the Neanderthal psychology. The dopamine deficiency leads to decreased melanin synthesis and fairness of the population. This was responsible for the fair colour of the Neanderthals.

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 neuropathology of autism and schizophrenia. Neanderthals consuming a ketogenic diet produces more of GABA an inhibitory neurotransmitter resulting in the docile quiet nature of the Neanderthals. 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. Cerebellum is responsible for intuitive, unconscious behaviour as well as creativity and spirituality. The cerebellum is the site of extrasensory perception, magical acts and hypnosis. The predominant homo sapiens had prefrontal cortex dominance over the cerebellum resulting in more of conscious behaviour. This

leads onto the ontogenesis of schizophrenia, autism and epilepsy.

The Neanderthals consuming a glucogenic diet produces increased glycolysis in the setting of PDH inhibition. This produces the Warburg phenotype. There is increased lymphocytic glycolysis producing autoimmune diseases and immune activation. The increased levels of GAPD result in nuclear cell death and neurodegeneration. The predominance of glycolysis and suppression of mitochondrial function results in glycemia and metabolic syndrome x. The increased mitochondrial PT pore hexokinase leads to cell proliferation and oncogenesis. The glycolytic intermediate 3-phosphoglycerate is converted to glycine resulting in NMDA excitotoxicity contributing to schizophrenia and autism. Cerebellar dominance is reported in schizophrenia, autism and epilepsy.

The cerebellar hyperplasia results in sympathetic hyperactivity and parasympathetic neuropathy. This contributes to oncogene activation. Vagal neuropathy results in immune activation and autoimmunity important in schizophrenia, autism and epilepsy. Vagal neuropathy and sympathetic overactivity can contribute to glycogenolysis and lipolysis resulting in insulin resistance. Insulin resistance leads to schizophrenia, autism and epilepsy. Cerebellar dominance and cerebellar cognitive affective dysfunction can contribute to schizophrenia and autism. The increased porphyrin synthesis resulting from succinyl CoA generated by GABA shunt and glycine generated by glycolysis contributes to increased extrasensory perception important in schizophrenia and autism. Sympathetic overactivity and parasympathetic neuropathy can contribute to schizophrenia, autism and epilepsy.

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 produces oncogene activation and NFKB activation resulting in schizophrenia, autism and epilepsy.

The increase in intracellular calcium opens the mitochondrial PT pore resulting in cell death of schizophrenia, autism and epilepsy. 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 can modulate the glutamatergic thalamo-cortico-thalamic pathway and consciousness resulting in schizophrenia, autism and epilepsy. Digoxin induced magnesium depletion can inhibit reverse transcriptase activity and HERV generation modulating the dynamicity of the genome. HERV expression has been related to schizophrenia, autism and epilepsy. 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. The dysfunction of this integrative phenomenon can lead to schizophrenia, autism and epilepsy. Digoxin functions as a Neanderthal master hormone.

The actinidic archaea are cholesterol catabolising and leads to low levels of testosterone and estrogen. This leads on to asexual features and low reproductive rates of the Neanderthal population. 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 concommitant 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. 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. This gender phenomenon can lead onto the ontogenesis of schizophrenia, autism and epilepsy.

The cholesterol catabolism results in cholesterol depletion and bile acid deficiency. Bile acids bind to VDR and are immunomodulatory. Bile acid deficiency leads to immune activation and autoimmunity in schizophrenia, autism and epilepsy. Bile acids bind to FXR, LXR and PXR modulating lipid and carbohydrate metabolism. This leads to insulin resistance in the presence of bile acid deficiency. Bile acid uncouples oxidative phosphorylation and its deficiency leads to insulin resistance. Insulin resistance is important in schizophrenia, autism and epilepsy. Schizophrenia is called as an insulin resistance state of the brain. Bile acids bind to olfactory receptors and are important in group identity. Bile acid deficiency leads to formation of small social groups in Neanderthals and genesis of autism. Cholesterol depletion also leads to vitamin D deficiency. Vitamin D binds to VDR and produces immunomodulation. Vitamin D deficiency leads to immune activation and autoimmunity in schizophrenia, autism and epilepsy. 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. All these lead to schizophrenia, autism and epilepsy.

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. This phenomenon leads to the ontogenesis of schizophrenia, autism and epilepsy.

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5

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.[1-16] The data is described in this paper.

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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6

Pathogenesis of Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease – Relation to Archaeal Mediated Rna Viroids and Amyloidosis

Introduction

Prion proteins have been implicated in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. The beta amyloid in Alzheimer's disease, alpha synuclein in Parkinson's disease, the TAR protein in frontotemporal dementia and copper zinc dismutase in motor neuron disease behaves like prion proteins. 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. Prion phenomena were initially described for Creutzfeldt Jakob's disease (CJD), but now it is found to be wide spread in chronic disease pathogenesis. Ribonucleoproteins are well known to behave like prion proteins and form amyloid. We have demonstrated actinidic archaea which secretes RNA viroids in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. 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 civilizational diseases like neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. 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: - neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron 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. 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. 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.

Results

The results show that there was increase in cytochrome F420 in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease indicating increased archaeal growth. There was also an increase in free RNA indicating self replicating RNA viroids in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. 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.

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
PD	23.46	1.87	59.27	8.86
AD	23.12	2.00	56.90	6.94
MND	22.06	1.61	57.81	6.04
F value	306.749		130.054	
P value	< 0.001		< 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
PD	23.08	1.87	65.09	3.48
AD	23.29	1.92	65.39	3.95
MND	23.11	1.52	66.68	3.97
F value	427.828		654.453	
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. 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. This can lead to neurodegenerations - Alzheimer's disease, Parkinson's

disease and motor neuron disease.

Amyloidogenesis has been implicated in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. The beta amyloid in Alzheimer's disease, alpha synuclein in Parkinson's disease, the TAR protein in frontotemporal dementia and copper zinc dismutase in motor neuron disease behaves like prion proteins. 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 neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease are due to actinidic archaeal generated RNA viroid induced prion protein generation and amyloidogenesis. Prion proteins have been implicated in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. The beta amyloid in Alzheimer's disease, alpha synuclein in Parkinson's disease, the TAR protein in frontotemporal dementia and copper zinc dismutase in motor neuron disease behaves like prion proteins. The present study shows that the same prion protein mechanism can operate in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. Sporadic CJD is also induced by actinidic archaea induced RNA viroids. Actinidic archaeal induced RNA viroids generated prions can be transferred between individuals indicating the infective nature of neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease.

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 neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. The widespread incidence of these systemic diseases leads to extinction of the neanderthalised species.

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7

Endosymbiotic Actinidic Archaeal Synthesis of Digoxin from Cholesterol Regulates Cellular Function and Contributes to the Pathogenesis of Systemic Lupus Erythematosis, Multiple Sclerosis and Rheumatoid Arthritis

Introduction

Actinides like rutile, endogenous digoxin as well as organisms like phytoplasmas and viroids have been implicated in the etiology of systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis.[1-4] Endogenous digoxin has been related to the pathogenesis of systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis.[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: - systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis. 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.

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
MS	22.12	1.81	61.33	9.82
SLE	22.29	1.66	59.02	7.50
RA	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
MS	0.52	0.03	0.214	0.032
SLE	0.56	0.05	0.220	0.052
RA	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 lead to the pathogenesis of systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis.

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 signalling lipid metabolism, cell growth and differentiation, apoptosis, neuronal transmission and euchromatin / heterochromatin expression. This can lead to the pathogenesis of systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis.

NMDA receptors can be modulated by digoxin induced calcium oscillations resulting NMDA excitotoxicity.[4] The dipolar 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] This can lead to perception of low level EMF contributing to the pathogenesis of systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis. The higher degree of integration of the archaea into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance.[4] Right hemispheric dominance can lead to systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis. The increased integration of archaea into the neuronal genome can produce increased digoxin mediated NMDA transmission producing systemic lupus erythematosis,

multiple sclerosis and rheumatoid arthritis. Digoxin induced calcium oscillations can activate NFKB producing immune activation and cytokine secretion. The archaeal digoxin induced chronic immune activation can lead on to autoimmune disease.[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 insulin resistance. The archaeal digoxin generated cytokines can lead to TNF alpha induced insulin resistance. Insulin resistance can lead to systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis. 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 channelling 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 systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis due to defective neuro-immuno-endocrine integration. 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 insulin resistance. Fat fuels insulin resistance by binding to the toll receptor and producing immune activation and immune infiltration of the adipose tissue.[4] Insulin resistance can lead to systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis. 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. Prion proteins and HERV sequences are related to systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis. Thus the archaeal digoxin can produce neuro-immune-metabolic-endocrine-genetic integration. The increased archaeal cholesterol catabolism and digoxin secretion can lead to diverse pathological states of systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis.

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8

Actinidic Archaea and Viroids Related Hepato-Gastrointestinal Syndrome

Introduction

Endomyocardial fibrosis (EMF) along with the root wilt disease of coconut is endemic to Kerala with its radioactive actinide beach sands. Actinides like cerium producing intracellular magnesium deficiency due to cerium-magnesium exchange sites in the cell membrane has been implicated in the etiology of EMF.[1] Endogenous digoxin, a steroidal glycoside which functions as a membrane sodium-potassium ATPase inhibitor has also been related to its etiology due to the intracellular magnesium deficiency it produces.[2] Organisms like phytoplasmas and viroids have also been demonstrated to play a role in the etiology of these diseases.[3, 4] Endogenous digoxin has been related to the pathogenesis of cirrhosis liver, ulcerative colitis, irritable bowel syndrome and peptic ulcer disease.[2] The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered.[5, 6, 7] Davies has put forward the concept of a shadow biosphere of organisms with alternate biochemistry present in earth itself.[8] An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described.[6]

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: - cirrhosis liver, ulcerative colitis, irritable bowel syndrome and peptic ulcer 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. 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+ciprofloxacin and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond.[9] 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, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids.[10-13] 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. The statistical analysis was done by ANOVA.

Results

The parameters checked as indicated above were: - cytochrome F420, free RNA, free DNA, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids. 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. 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 cerium and antibiotics on muramic acid and serotonin.*

Group	Muramic acid % change (Increase with Cerium)		Muramic acid % change (Decrease with Doxy+Cipro)		5 HT % (Increase without Doxy)		5 HT % (Decrease with Doxy)	
	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
Cirrhosis	23.11	1.82	66.96	3.79	23.13	1.78	64.88	4.96
PUD	23.43	1.59	65.71	4.01	22.92	1.71	65.58	4.74
UC	23.81	1.45	66.85	3.72	22.83	1.96	63.42	5.10
IBS	23.28	1.95	66.02	3.90	22.79	1.79	62.70	5.05
F value	403.394		680.284		348.867		364.999	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	DNA % change (Increase with Cerium)		DNA % change (Decrease with Doxy)		RNA % change (Increase with Cerium)		RNA % change (Decrease with Doxy)	
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
Cirrhosis	22.78	1.94	63.06	6.20	22.91	1.69	66.23	3.44
PUD	23.07	1.50	62.99	5.27	23.32	1.92	66.07	4.11
UC	23.28	1.93	61.81	2.75	22.89	1.85	66.33	3.73
IBS	23.61	1.53	67.77	3.23	22.94	1.88	65.84	4.20
F value	337.577		356.621		427.828		654.453	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 3. *Effect of cerium and antibiotics on HMG CoA reductase and PAH.*

Group	HMG CoA R % change (Increase with Cerium)		HMG CoA R % change (Decrease with Doxy)		PAH % change (Increase with Cerium)		PAH % change (Decrease with Doxy)	
Normal	4.30	0.20	18.35	0.35	4.45	0.14	18.25	0.72
Cirrhosis	23.29	1.67	59.19	7.18	23.39	1.63	65.88	5.01
PUD	23.56	1.83	63.61	6.60	23.06	1.56	64.49	4.64
UC	23.24	1.79	63.55	8.01	23.49	1.48	64.96	5.02
IBS	23.66	1.47	66.11	6.52	23.32	1.46	62.95	7.18
F value	319.332		199.553		391.318		257.996	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	Digoxin (ng/ml) (Increase with Cerium)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		Bile acids % change (Increase with Cerium)		Bile acids % change (Decrease with Doxy)	
Normal	0.11	0.00	0.054	0.003	4.29	0.18	18.15	0.58
Cirrhosis	0.50	0.06	0.206	0.034	22.08	1.76	64.20	5.16
PUD	0.50	0.05	0.223	0.025	22.72	1.76	61.84	7.63
UC	0.49	0.06	0.230	0.034	22.30	1.76	62.76	7.49
IBS	0.51	0.06	0.221	0.030	22.62	1.89	63.41	8.47
F value	135.116		71.706		290.441		203.651	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	Pyruvate % change (Increase with Cerium)		Pyruvate % change (Decrease with Doxy)		Hexokinase % change (Increase with Cerium)		Hexokinase % change (Decrease with Doxy)	
Normal	4.34	0.21	18.43	0.82	4.21	0.16	18.56	0.76
Cirrhosis	21.52	2.26	60.42	7.65	21.70	1.90	65.26	5.62
PUD	21.29	2.38	57.56	8.70	22.80	2.33	64.43	5.74
UC	21.34	2.24	60.25	8.94	22.29	2.22	65.14	5.66
IBS	20.74	1.47	61.98	6.44	22.36	2.40	63.46	5.69
F value	321.255		115.242		292.065		317.966	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	H_2O_2 % (Increase with Cerium)		H_2O_2 % (Decrease with Doxy)		ALA % (Increase with Cerium)		ALA % (Decrease with Doxy)	
Normal	4.43	0.19	18.13	0.63	4.40	0.10	18.48	0.39
Cirrhosis	23.46	1.61	61.77	6.79	23.98	1.72	66.76	4.01
PUD	22.38	1.65	64.59	7.12	23.52	1.74	67.75	3.43
UC	23.65	1.11	59.37	6.93	23.13	1.96	65.86	3.83
IBS	23.22	1.76	59.12	5.14	23.32	1.95	66.69	3.91
F value	380.721		171.228		372.716		556.411	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 7. *Effect of cerium and antibiotics on ATP synthase and cytochrome F 420.*

Group	ATP synthase % (Increase with Cerium)		ATP synthase % (Decrease with Doxy)		CYT F420 % (Increase with Cerium)		CYT F420 % (Decrease with Doxy)	
Normal	4.40	0.11	18.78	0.11	4.48	0.15	18.24	0.66
Cirrhosis	23.27	1.56	66.43	3.77	22.46	2.39	61.42	7.26
PUD	23.09	1.43	66.43	4.07	22.41	2.02	60.47	8.32
UC	23.14	1.80	66.40	3.64	22.95	1.53	58.86	6.97
IBS	23.16	1.31	67.28	3.54	22.52	1.33	61.43	11.16
F value	449.503		673.081		306.749		130.054	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Abbreviations

PUD: Peptic ulcer disease

UC: Ulcerative colitis

IBS: Irritable bowel syndrome

Discussion

There was increase in cytochrome F420 indicating archaeal growth in cirrhosis

liver, ulcerative colitis, irritable bowel syndrome and peptic ulcer disease. The archaea can synthesise and use cholesterol as a carbon and energy source.[14, 15] 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 cerium induced increase in enzyme activities.[16] 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.[7] The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide.[15] 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.[17] 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.[18] 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.[19] 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.[20] 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.[21] The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites.[20, 21] This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters.[22] The viroidal complementary DNA can function as jumping genes producing a dynamic genome important in HLA gene expression. This modulation of HLA gene expression by viroidal complementary DNA can result in immune activation. The RNA viroids can regulate mRNA function by RNA interference.[19] The phenomena of RNA interference can modulate T cell and B cell function and euchromatin/heterochromatin expression. RNA viroidal mRNA interference related immune activation plays a role in the pathogenesis of cirrhosis liver, ulcerative colitis, irritable bowel syndrome and peptic ulcer disease.

The presence of muramic acid, HMG CoA reductase and cholesterol oxidase activity inhibited by antibiotics indicates the presence of bacteria with mevalonate pathway. The bacterial with mevalonate pathway include streptococcus, staphylococcus, actinomycetes, listeria, coxiella and borrelia.[23] The bacteria and archaea with mevalonate pathway and cholesterol catabolism had a evolutionarily advantage and constitutes the isoprenoidal clade organism with the archaea evolving into mevalonate pathway gram positive and gram negative organism through horizontal gene transfer of viroidal and virus genes.[24] The isoprenoidal clade prokaryotes develop into other groups of prokaryotes via viroidal/virus as well as eukaryotic horizontal gene transfer producing bacterial speciation.[25] 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 eukaryotic and human genes resulting in viral speciation. Bacterial and 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 prokaryotic and viral speciation. The multicellular eukaryote developed so that their endosymbiotic archaeal colonies could survive and forage better. The multicellular eukaryotes are like bacterial biofilms. The archaea and bacteria with a mevalonate pathway uses the extracellular RNA viroids and DNA viroids for quorum sensing and in the generation of symbiotic biofilm like structures which develop into multicellular eukaryotes.[26, 27] The endosymbiotic archaea and bacteria with mevalonate pathway still uses the RNA viroids and DNA viroids for the regulation of muticellular eukaryote. Pollution is induced by the primitive nanoarchaea and mevalonate pathway bacteria synthesised 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.[28] 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. Bacteria and viruses have been related to the pathogenesis of cirrhosis liver, ulcerative colitis, irritable bowel syndrome and peptic ulcer disease.[29, 30] Helicobacter pylori has been related to the pathogenesis of peptic ulcer disease.[29] Mollicutes, atypical mycobacteria and enterobacteria has been implicated in inflammatory bowel

disease.[29, 30] Gut bacteria and endotoxinemia contributes to the pathogenesis of cirrhosis liver.[29] Gut bacteria also plays a role in irritable bowel syndrome.[29] The change in the length and grammar of the noncoding region produces eukaryotic speciation and individuality.[31] Changes in the length of noncoding region especially human endogenous retroviruses can lead onto autoimmune diseases.[32] 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 or microchimeras leading to human diseases like cirrhosis liver, ulcerative colitis, irritable bowel syndrome and peptic ulcer disease. The microchimeras formed can lead to autoantigens, immune activation and autoimmune pathology. Autoimmunity has been described in inflammatory bowel disease.[29]

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 signalling can activate NFKB producing chronic immune activation[2, 33]. The archaeal cholesterol aromatase generated PAH can produce immune activation. The archaea and viroid induced chronic immune activation and generation of superantigens can lead on to autoimmune disease and immune activation. Immune activation has been related to the pathogenesis of cirrhosis liver, ulcerative colitis, irritable bowel syndrome and peptic ulcer disease.[29, 30]

The archaea and viroids can regulate the nervous system including the NMDA synaptic transmission.[2] NMDA can be activated by digoxin induced calcium oscillations, PAH and viroid induced RNA interference[2]. The cholesterol ring

oxidase generated pyruvate can be converted by the GABA shunt pathway to glutamate. The archaeal cholesterol aromatase can generate serotonin.[17] Glutamatergic and serotoninergic transmission can lead to immune activation which is important in the pathogenesis of cirrhosis liver, ulcerative colitis, irritable bowel syndrome and peptic ulcer disease. Monoamine neurotransmitters and glutamate have been implicated in abnormal gut motility of irritable bowel syndrome. The higher degree of integration of the archaea into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance.[2] Right hemispheric dominance can lead to cirrhosis liver, ulcerative colitis, irritable bowel syndrome and peptic ulcer disease.[2]

Archaea, viroids and digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype.[34] 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. The lymphocytes depend on glycolysis for their energy needs. The increased glycolysis induced by the Warburg phenotype leads to immune activation. Lactic acid generated by increased glycolysis leads to immune stimulation. Immune activation as noted before is important in the pathogenesis of cirrhosis liver, ulcerative colitis, irritable bowel syndrome and peptic ulcer disease. Cholesterol oxidase activity, increased glycolysis related NADPH oxidase activity, bacterial porphyrin induced redox stress and mitochondrial dysfunction generates free radicals important in the pathogenesis of cirrhosis liver, ulcerative colitis, irritable bowel syndrome and peptic ulcer disease. 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.[34] 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 channelling to the mevalonate pathway. The archaeal cholesterol catabolism can deplete the lymphocytic cell membranes of cholesterol resulting in alteration of lymphocytic cell membrane microdomains related receptors producing immune activation. Hyperdigoxinemia is important in the pathogenesis of cirrhosis liver, ulcerative colitis, irritable bowel syndrome and peptic ulcer disease.[2] Digoxin can increase lymphocytic intracellular calcium which leads on to induction of NFKB and immune activation.[2] The archaeal bile acids can bind GPCR and modulate D2 regulating the conversion of T4 to T3. T3 activates uncoupling proteins reducing redox stress. Bile acids can also activate NRF ½ inducing NQO1, GST, HOI reducing redox stress. Bile acids can bind PXR inducing the bile acid shunt pathway of cholesterol detoxification. Bile acids can bind macrophage GPCR and VDR producing immunosuppression and inhibiting NFKB. This helps to modulate the archaea and viroid induced chronic immune activation. Bile acids are thus protective compounds and put a break on the archaea and viroid induced changes.[35] Thus the actinide, viroid and mevalonate pathway bacteria induced metabolic, genetic, immune and neuronal transmission changes can lead onto cirrhosis liver, ulcerative colitis, irritable bowel syndrome and peptic ulcer disease.

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9

A Cholesterol and Actinide Dependent Shadow Biosphere of Archaea and Viroids in Pulmonary Diseases

Introduction

Endomyocardial fibrosis (EMF) along with the root wilt disease of coconut is endemic to Kerala with its radioactive actinide beach sands. Actinides like rutile producing intracellular magnesium deficiency due to rutile-magnesium exchange sites in the cell membrane has been implicated in the etiology of EMF.[1] Endogenous digoxin, a steroidal glycoside which functions as a membrane sodium-potassium ATPase inhibitor has also been related to its etiology due to the intracellular magnesium deficiency it produces.[2] Organisms like phytoplasmas and viroids have also been demonstrated to play a role in the etiology of these diseases.[3, 4] Endogenous digoxin has been related to the pathogenesis of interstitial lung disease, chronic bronchitis emphysema and bronchial asthma.[2] The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered.[5, 6, 7] Davies has put forward the concept of a shadow biosphere of organisms with alternate biochemistry present in earth itself.[8] An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described.[6]

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: - interstitial lung disease, chronic bronchitis emphysema and bronchial asthma. 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.[9] 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, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA redutase, digoxin and bile acids.[10-13] 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. The statistical analysis was done by ANOVA.

Results

The parameters checked as indicated above were:- cytochrome F420, free RNA, free DNA, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids. 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 muramic acid and serotonin.*

Group	Muramic acid % change (Increase with Rutile)		Muramic acid % change (Decrease with Doxy+Cipro)		5 HT % (Increase without Doxy)		5 HT % (Decrease with Doxy)	
	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
ASTH	23.45	1.79	66.32	3.63	22.56	2.46	62.70	4.53
CBE	23.20	1.57	66.65	4.26	22.12	2.44	63.69	5.14
ILD	22.95	1.61	65.76	4.01	22.92	1.99	66.55	4.55
F value	403.394		680.284		348.867		364.999	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy)	
	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
ASTH	23.17	1.49	63.96	5.72	23.21	1.72	66.40	3.69
CBE	22.98	1.50	65.13	4.87	23.15	1.62	66.48	4.17
ILD	22.79	2.20	64.26	6.02	22.60	1.64	66.86	4.21
F value	337.577		356.621		427.828		654.453	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	HMG CoA R % change (Increase with Rutile)		HMG CoA R % change (Decrease with Doxy)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.30	0.20	18.35	0.35	4.45	0.14	18.25	0.72
ASTH	22.03	2.58	60.73	5.55	23.22	1.67	62.06	2.05
CBE	22.28	2.10	65.21	3.81	23.31	1.70	64.38	5.67
ILD	22.75	2.75	62.71	6.04	22.98	2.01	63.91	4.86
F value	319.332		199.553		391.318		257.996	
P value	< 0.001		< 0.001		< 0.001		< 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)	
	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
ASTH	0.49	0.07	0.199	0.022	23.38	2.13	64.52	6.49
CBE	0.55	0.04	0.219	0.038	23.19	1.72	64.25	6.19
ILD	0.50	0.07	0.183	0.029	22.77	1.97	64.79	5.78
F value	135.116		71.706		290.441		203.651	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy)		Hexokinase % change (Increase with Rutile)		Hexokinase % change (Decrease with Doxy)	
	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
ASTH	21.26	2.04	55.44	7.92	22.20	2.41	64.44	5.78
CBE	21.53	2.15	58.30	8.80	22.90	2.07	67.17	4.33
ILD	20.89	2.28	58.84	9.44	22.54	2.57	65.57	5.41
F value	321.255		115.242		292.065		317.966	
P value	< 0.001		< 0.001		< 0.001		< 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)		ALA % (Increase with Rutile)		ALA % (Decrease with Doxy)	
	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
ASTH	22.90	1.51	63.27	4.96	23.43	1.57	66.30	3.57
CBE	23.43	1.74	64.28	7.33	22.76	2.20	67.63	3.52
ILD	23.30	1.47	60.35	7.93	22.63	1.63	67.24	3.42
F value	380.721		171.228		372.716		556.411	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 7. *Effect of rutile and antibiotics on ATP synthase and cytochrome F 420.*

Group	ATP synthase % (Increase with Rutile)		ATP synthase % (Decrease with Doxy)		CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.40	0.11	18.78	0.11	4.48	0.15	18.24	0.66
ASTH	22.94	1.94	66.18	4.15	22.39	1.75	64.24	8.55
CBE	23.32	1.74	65.67	4.16	22.78	2.23	62.58	8.62
ILD	23.33	1.35	66.83	3.27	21.95	1.56	53.17	7.20
F value	449.503		673.081		306.749		130.054	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth in interstitial lung disease, chronic bronchitis emphysema and bronchial asthma. The archaea can synthesise and use cholesterol as a carbon and energy source.[14, 15] 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.[16] 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.[7] The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide.[15] 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.[17] 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.[18] 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.[19] 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.[20] 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.[21] The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites.[20, 21] This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters.[22] The viroidal complementary DNA can function as jumping genes producing a dynamic genome important in HLA gene expression. This modulation of HLA gene expression by viroidal complementary DNA can result in autoimmune diseases. The RNA viroids can regulate mrna function by RNA interference.[19] The phenomena of RNA interference can modulate T cell and B cell function and euchromatin/heterochromatin expression. RNA viroidal mRNA interference plays a role in the pathogenesis of autoimmune diseases like interstitial lung disease, chronic bronchitis emphysema and bronchial asthma.

The presence of muramic acid, HMG CoA reductase and cholesterol oxidase activity inhibited by antibiotics indicates the presence of bacteria with mevalonate pathway. The bacterial with mevalonate pathway include streptococcus,

staphylococcus, actinomycetes, listeria, coxiella and Borrelia.[23] The bacteria and archaea with mevalonate pathway and cholesterol catabolism had a evolutionarily advantage and constitutes the isoprenoidal clade organism with the archaea evolving into mevalonate pathway gram positive and gram negative organism through horizontal gene transfer of viroidal and virus genes.[24] The isoprenoidal clade prokaryotes develop into other groups of prokaryotes via viroidal/virus as well as eukaryotic horizontal gene transfer producing bacterial speciation.[25] 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 eukaryotic and human genes resulting in viral speciation. Bacterial and 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 prokaryotic and viral speciation. The multicellular eukaryote developed so that their endosymbiotic archaeal colonies could survive and forage better. The multicellular eukaryotes are like bacterial biofilms. The archaea and bacteria with a mevalonate pathway uses the extracellular RNA viroids and DNA viroids for quorum sensing and in the generation of symbiotic biofilm like structures which develop into multicellular eukaryotes.[26, 27] The endosymbiotic archaea and bacteria with mevalonate pathway still uses the RNA viroids and DNA viroids for the regulation of muticellular eukaryote. Pollution is induced by the primitive nanoarchaea and mevalonate pathway bacteria synthesised 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.[28] 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

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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 signalling can activate NFKB producing chronic immune activation.[2, 33] The archaeal cholesterol aromatase generated PAH can produce immune activation. The archaea and viroid induced chronic immune activation and generation of superantigens can lead on to autoimmune disease. Immune activation has been related to the pathogenesis of interstitial lung disease, chronic bronchitis

emphysema and bronchial asthma.[29, 30] PAH has also been related to the pathogenesis of interstitial lung disease, chronic bronchitis emphysema and bronchial asthma.

The archaea and viroids can regulate the nervous system including the NMDA synaptic transmission.[2] NMDA can be activated by digoxin induced calcium oscillations, PAH and viroid induced RNA interference.[2] The cholesterol ring oxidase generated pyruvate can be converted by the GABA shunt pathway to glutamate. The archaeal cholesterol aromatase can generate serotonin.[17] Glutamatergic and serotoninergic transmission can lead to immune activation. Serotonin can produce bronchospasm leading onto bronchial asthma. The higher degree of integration of the archaea into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance.[2] Right hemispheric dominance can lead to autoimmune diseases like interstitial lung disease, chronic bronchitis emphysema and bronchial asthma.[2]

Archaea, viroids and digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype.[34] 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. The lymphocytes depend on glycolysis for their energy needs. The increased glycolysis induced by the Warburg phenotype leads to immune activation. Lactic acid generated by increased glycolysis leads to immune stimulation. Cholesterol oxidase activity, increased glycolysis related NADPH oxidase activity, bacterial porphyrin induced redox stress and mitochondrial dysfunction generates free radicals important in the pathogenesis of interstitial lung disease, chronic

bronchitis emphysema and bronchial asthma. 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.[34] 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 channelling to the mevalonate pathway. Hyperdigoxinemia is important in the pathogenesis of autoimmune diseases like interstitial lung disease, chronic bronchitis emphysema and bronchial asthma.[2] Digoxin can increase lymphocytic intracellular calcium which leads on to induction of NFKB and immune activation.[2] The archaeal cholesterol atabolism can deplete the lymphocytic cell membranes of cholesterol resulting in alteration of lymphocytic cell membrane microdomains related receptors producing immune activation. The archaeal bile acids can bind GPCR and modulate D2 regulating the conversion of T4 to T3. T3 activates uncoupling proteins reducing redox stress. Bile acids can also activate NRF ½ inducing NQO1, GST, HOI reducing redox stress. Bile acids can bind PXR inducing the bile acid shunt pathway of cholesterol detoxification. Bile acids can bind macrophage GPCR and VDR producing immunosuppression and inhibiting NFKB. This helps to modulate the archaea and viroid induced chronic immune activation. Bile acids are thus protective compounds and put a break on the archaea and viroid induced changes.[35] Thus the actinide, viroid and mevalonate pathway bacteria induced metabolic, genetic, immune and neuronal transmission changes can lead onto interstitial lung disease, chronic bronchitis emphysema and bronchial asthma.

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10

A Cholesterol and Actinide Dependent Shadow Biosphere of Archaea and Viroids in Chronic Renal Failure

Introduction

Endomyocardial fibrosis (EMF) along with the root wilt disease of coconut is endemic to Kerala with its radioactive actinide beach sands. Actinides like rutile producing intracellular magnesium deficiency due to rutile-magnesium exchange sites in the cell membrane has been implicated in the etiology of EMF.[1] Endogenous digoxin, a steroidal glycoside which functions as a membrane sodium-potassium ATPase inhibitor has also been related to its etiology due to the intracellular magnesium deficiency it produces.[2] Organisms like phytoplasmas and viroids have also been demonstrated to play a role in the etiology of these diseases.[3, 4] Endogenous digoxin has been related to the pathogenesis of chronic renal failure- chronic glomerulonephritis.[2] The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered.[5, 6, 7] Davies has put forward the concept of a shadow biosphere of organisms with alternate biochemistry present in earth itself.[8] An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described.[6]

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: - chronic renal failure-chronic glomerulonephritis. 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.[9] 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, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids.[10-13] 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. The statistical analysis was done by ANOVA.

Results

The parameters checked as indicated above were:- cytochrome F420, free RNA, free DNA, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids. 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 muramic acid and serotonin.*

Group	Muramic acid % change (Increase with Rutile)		Muramic acid % change (Decrease with Doxy+Cipro)		5 HT % (Increase without Doxy)		5 HT % (Decrease with Doxy)	
	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
CRF	23.41	1.55	66.36	4.31	23.49	1.19	64.63	6.58
F value	403.394		680.284		348.867		364.999	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy)	
	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
CRF	22.52	2.06	66.09	5.73	23.34	1.58	65.76	3.91
F value	337.577		356.621		427.828		654.453	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	HMG CoA R % change (Increase with Rutile)		HMG CoA R % change (Decrease with Doxy)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.30	0.20	18.35	0.35	4.45	0.14	18.25	0.72
CRF	23.88	1.68	63.69	7.06	23.69	1.57	66.86	3.61
F value	319.332		199.553		391.318		257.996	
P value	< 0.001		< 0.001		< 0.001		< 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)	
	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
CRF	0.51	0.06	0.192	0.035	23.29	1.41	62.44	7.64
F value	135.116		71.706		290.441		203.651	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy)		Hexokinase % change (Increase with Rutile)		Hexokinase % change (Decrease with Doxy)	
	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
CRF	21.00	2.02	61.03	7.33	22.95	1.49	65.72	4.58
F value	321.255		115.242		292.065		317.966	
P value	< 0.001		< 0.001		< 0.001		< 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)		ALA % (Increase with Rutile)		ALA % (Decrease with Doxy)	
	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
CRF	22.63	2.02	58.08	6.30	24.00	1.64	66.04	4.36
F value	380.721		171.228		372.716		556.411	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 7. *Effect of rutile and antibiotics on ATP synthase and cytochrome F 420.*

Group	ATP synthase % (Increase with Rutile)		ATP synthase % (Decrease with Doxy)		CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.40	0.11	18.78	0.11	4.48	0.15	18.24	0.66
CRF	23.22	1.35	66.42	4.21	22.46	1.75	63.22	8.22
F value	449.503		673.081		306.749		130.054	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Abbreviations

CRF: Chronic renal failure

Discussion

There was increase in cytochrome F420 indicating archaeal growth in chronic renal failure-chronic glomerulonephritis. The archaea can synthesise and use cholesterol as a carbon and energy source.[14, 15] 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.[16] 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.[7] The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide.[15] 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.[17] 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.[18] 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.[19] 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.[20] 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.[21] The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites.[20, 21] This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters.[22] The viroidal complementary DNA can function as jumping genes producing a dynamic genome important in HLA gene expression. This modulation of HLA gene expression by viroidal complementary DNA can result in immune activation. The RNA viroids can regulate mRNA function by RNA interference.[19] The phenomena of RNA interference can modulate T cell and B cell function and euchromatin/heterochromatin expression. RNA viroidal mRNA interference plays a role in the pathogenesis of chronic renal failure- chronic glomerulonephritis due to immune activation.

The presence of muramic acid, HMG CoA reductase and cholesterol oxidase activity inhibited by antibiotics indicates the presence of bacteria with mevalonate pathway. The bacterial with mevalonate pathway include streptococcus, staphylococcus, actinomycetes, listeria, coxiella and borrelia.[23] The bacteria and archaea with mevalonate pathway and cholesterol catabolism had a evolutionarily advantage and constitutes the isoprenoidal clade organism with the archaea evolving into mevalonate pathway gram positive and gram negative organism through horizontal gene transfer of viroidal and virus genes.[24] The isoprenoidal clade prokaryotes develop into other groups of prokaryotes via viroidal/virus as well as eukaryotic horizontal gene transfer producing bacterial speciation.[25] 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 eukaryotic and human genes resulting in viral speciation. Bacterial and 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 prokaryotic and viral speciation. The multicellular eukaryote developed so that their endosymbiotic archaeal colonies could survive and forage better. The multicellular eukaryotes are like bacterial biofilms. The archaea and bacteria with a mevalonate pathway uses the extracellular RNA viroids and DNA viroids for quorum sensing and in the generation of symbiotic biofilm like structures which develop into multicellular eukaryotes.[26, 27] The endosymbiotic archaea and bacteria with mevalonate pathway still uses the RNA viroids and DNA viroids for the regulation of muticellular eukaryote. Pollution is induced by the primitive nanoarchaea and mevalonate pathway bacteria synthesised 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.[28] 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. Bacteria and viruses have been related to the pathogenesis of chronic renal failure-chronic glomerulonephritis.[29, 30] The change in the length and grammar of the noncoding

region produces eukaryotic speciation and individuality.[31] Changes in the length of noncoding region especially human endogenous retroviruses can lead onto immune activation and autoimmune diseases.[32] 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 or microchimeras leading to human diseases like chronic renal failure-chronic glomerulonephritis. The microchimeras formed can lead to autoantigens and immune activation resulting in chronic renal failure-chronic glomerulonephritis.

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 signalling can activate NFKB producing chronic immune activation.[2, 33] The archaeal cholesterol aromatase generated PAH can produce immune activation. The archaea and viroid induced chronic immune activation and generation of superantigens can lead on to immune activation and autoimmune disease. Immune activation has been related to the pathogenesis of chronic renal failure-chronic glomerulonephritis.[29, 30]

The archaea and viroids can regulate the nervous system including the NMDA synaptic transmission.[2] NMDA can be activated by digoxin induced calcium oscillations, PAH and viroid induced RNA interference.[2] The cholesterol ring oxidase generated pyruvate can be converted by the GABA shunt pathway to glutamate. The archaeal cholesterol aromatase can generate serotonin.[17] Glutamatergic and serotoninergic transmission can lead to immune activation. Immune activation mediated by neurotransmitters can contribute to chronic renal

failure-chro failure nic glomerulonephritis. The higher degree of integration of the archaea into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance.[2] Right hemispheric dominance can lead to chronic renal failure-chronic glomerulonephritis.[2]

Archaea, viroids and digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype.[34] 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. The lymphocytes depend on glycolysis for their energy needs. The increased glycolysis induced by the Warburg phenotype leads to immune activation. Lactic acid generated by increased glycolysis leads to immune stimulation. Immune activation consequent to the generation of the Warburg phenotype can lead to chronic renal failure-chronic glomerulonephritis. Cholesterol oxidase activity, increased glycolysis related NADPH oxidase activity, bacterial porphyrin induced redox stress and mitochondrial dysfunction generates free radicals important in the pathogenesis of chronic renal failure-chronic glomerulonephritis. 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.[34] 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 channelling to the mevalonate pathway. Hyperdigoxinemia is important in the pathogenesis of chronic renal failure-chronic glomerulonephritis.[2] Digoxin can increase lymphocytic intracellular calcium which leads on to induction of NFKB and immune activation.[2] The archaeal cholesterol catabolism can deplete the

lymphocytic cell membranes of cholesterol resulting in alteration of lymphocytic cell membrane microdomains related receptors producing immune activation. Digoxin and membrane cholesterol depletion induced immune activation can contribute to chronic renal failure- chronic glomerulonephritis. The archaeal bile acids can bind GPCR and modulate D2 regulating the conversion of T4 to T3. T3 activates uncoupling proteins reducing redox stress. Bile acids can also activate NRF ½ inducing NQO1, GST, HOI reducing redox stress. Bile acids can bind PXR inducing the bile acid shunt pathway of cholesterol detoxification. Bile acids can bind macrophage GPCR and VDR producing immunosuppression and inhibiting NFKB. This helps to modulate the archaea and viroid induced chronic immune activation. Bile acids are thus protective compounds and put a break on the archaea and viroid induced changes.[35] Thus the actinide, viroid and mevalonate pathway bacteria induced metabolic, genetic, immune and neuronal transmission changes can lead onto chronic renal failure-chronic glomerulonephritis.

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11

A Cholesterol and Actinide Dependent Shadow Biosphere of Archaea and Viroids in Retroviral and Prion Disease

Introduction

Endomyocardial fibrosis (EMF) along with the root wilt disease of coconut is endemic to Kerala with its radioactive actinide beach sands. Actinides like rutile producing intracellular magnesium deficiency due to rutile-magnesium exchange sites in the cell membrane has been implicated in the etiology of EMF.[1] Endogenous digoxin, a steroidal glycoside which functions as a membrane sodium-potassium ATPase inhibitor has also been related to its etiology due to the intracellular magnesium deficiency it produces.[2] Organisms like phytoplasmas and viroids have also been demonstrated to play a role in the etiology of these diseases.[3, 4] Endogenous digoxin has been related to the pathogenesis of acquired immunodeficiency syndrome and creutzfeldt jakob disease.[2] The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered.[5, 6, 7] Davies has put forward the concept of a shadow biosphere of organisms with alternate biochemistry present in earth itself.[8] An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described.[6]

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: - acquired immunodeficiency syndrome and creutzfeldt jakob 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. 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.[9] 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, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids.[10, 11, 12, 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. The statistical analysis was done by ANOVA.

Results

The parameters checked as indicated above were: - cytochrome F420, free RNA, free DNA, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids. 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 muramic acid and serotonin.*

Group	Muramic acid % change (Increase with Rutile)		Muramic acid % change (Decrease with Doxy+Cipro)		5 HT % (Increase without Doxy)		5 HT % (Decrease with Doxy)	
	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
AIDS	23.43	1.57	66.30	3.57	22.98	1.50	65.13	4.87
CJD	23.70	1.75	68.06	3.52	23.81	1.49	64.89	6.01
F value	403.394		680.284		348.867		364.999	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy)	
	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
AIDS	22.56	2.46	62.70	4.53	23.32	1.74	65.67	4.16
CJD	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	

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

Group	HMG CoA R % change (Increase with Rutile)		HMG CoA R % change (Decrease with Doxy)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.30	0.20	18.35	0.35	4.45	0.14	18.25	0.72
AIDS	22.86	2.58	66.53	5.59	23.23	1.97	65.89	5.05
CJD	22.38	2.38	60.65	5.27	23.46	1.91	61.56	4.61
F value	319.332		199.553		391.318		257.996	
P value	< 0.001		< 0.001		< 0.001		< 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)	
	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
AIDS	0.56	0.05	0.220	0.052	22.29	1.47	64.35	5.58
CJD	0.53	0.06	0.212	0.045	23.30	1.88	62.49	7.26
F value	135.116		71.706		290.441		203.651	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy)		Hexokinase % change (Increase with Rutile)		Hexokinase % change(Decrease with Doxy)	
	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
AIDS	21.21	2.36	58.73	8.10	21.11	2.25	64.20	5.38
CJD	21.07	1.79	63.90	7.13	22.47	2.17	65.97	4.62
F value	321.255		115.242		292.065		317.966	
P value	< 0.001		< 0.001		< 0.001		< 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)		ALA % (Increase with Rutile)		ALA % (Decrease with Doxy)	
	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
AIDS	23.32	1.71	63.15	7.62	23.45	1.79	66.32	3.63
CJD	22.86	1.91	63.66	6.88	23.17	1.88	68.53	2.65
F value	380.721		171.228		372.716		556.411	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 7. *Effect of rutile and antibiotics on ATP synthase and cytochrome F 420.*

Group	ATP synthase % (Increase with Rutile)		ATP synthase % (Decrease with Doxy)		CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.40	0.11	18.78	0.11	4.48	0.15	18.24	0.66
AIDS	23.15	1.62	66.48	4.17	22.29	1.66	59.02	7.50
CJD	23.00	1.64	66.67	4.21	22.06	1.61	57.81	6.04
F value	449.503		673.081		306.749		130.054	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth in acquired immunodeficiency syndrome and creutzfeldt jakob disease. The archaea can synthesise and use cholesterol as a carbon and energy source.[14, 15] 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.[16] 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.[7] The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide.[15] 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.[17] 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.[18] 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.[19] 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.[20] 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.[21] The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites.[20, 21] This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters.[22] The viroidal complementary DNA can function as jumping genes producing a dynamic genome modulating DNA transcription. The RNA viroids can regulate mRNA function by RNA interference.[19] 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. The RNA viroids can recombine with HERV sequences and get encapsulated in microvesicles contributing to the retroviral state. Prion proteins can bind nucleic acids. The prion protein conformation is modulated by RNA viroid binding resulting in prion disease. RNA viroid induced mRNA interference can contribute to cell death in AIDS dementia, malignant transformation and autoimmunity in the acquired immunodeficiency syndrome.

The presence of muramic acid, HMG CoA reductase and cholesterol oxidase activity inhibited by antibiotics indicates the presence of bacteria with mevalonate pathway. The bacterial with mevalonate pathway include streptococcus, staphylococcus, actinomycetes, listeria, coxiella and borrelia.[23] The bacteria and archaea with mevalonate pathway and cholesterol catabolism had a evolutionarily advantage and constitutes the isoprenoidal clade organism with the archaea evolving into mevalonate pathway gram positive and gram negative organism through horizontal gene transfer of viroidal and virus genes.[24, 25] The isoprenoidal clade prokaryotes develop into other groups of prokaryotes via viroidal/virus as well as eukaryotic horizontal gene transfer producing bacterial speciation.[26] 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 eukaryotic and human genes resulting in viral speciation. Bacterial and 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 prokaryotic and viral speciation. The multicellular eukaryote developed so that their endosymbiotic archaeal colonies could survive and forage better. The multicellular eukaryotes are like bacterial biofilms. The archaea and bacteria with a mevalonate pathway uses the extracellular RNA viroids and DNA 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 and DNA viroids for the regulation of muticellular eukaryote. Pollution is induced by the primitive nanoarchaea and mevalonate pathway bacteria synthesised 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. Bacteria and viruses have been related to the pathogenesis of acquired immunodeficiency syndrome and creutzfeldt jakob disease. Mycoplasmas have been described as co-factors in HIV infection.[30] Mycoplasma infection of the cell can result in expression of HERV sequences. Changes in the length of noncoding region especially human endogenous retroviruses and the expression of HERV sequences can contribute to the pathogenesis of AIDS syndrome.[31] The change in the length and grammar of the noncoding region produces eukaryotic speciation and individuality.[32] 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 or microchimera leading to human diseases like acquired immunodeficiency syndrome and creutzfeldt jakob disease. The microchimera produces polyploidy which has been related to malignant transformation, autoimmune disease and neuronal degeneration like AIDS dementia described in acquired immunodeficiency syndrome.

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.[2, 33] The archaea and viroid can induce chronic immune activation and generation of superantigens. Chronic immune activation can lead onto an increase in CD_4 receptor and chemokine receptor density producing a predilection to develop acquired immunodeficiency syndrome. The generation of superantigens leads to autoimmunity and increased incidence of autoimmune vasculitis and arthritis common in AIDS. The archaea and viroids can regulate the nervous system including the NMDA synaptic transmission.[2] NMDA can be activated by digoxin induced calcium oscillations, PAH and viroid induced RNA interference.[2] The cholesterol ring oxidase generated pyruvate can be converted by the GABA shunt pathway to glutamate. The archaeal cholesterol aromatase can generate serotonin.[17] Glutamatergic and serotoninergic transmission can lead to immune activation important in the pathogenesis of AIDS. NMDA excitotoxicity and neurotransmitter induced immune activation can lead onto AIDS dementia. The increased generation of serotonin and dopamine from bacterial cholesterol catabolism can lead to mood disorders and schizophreniform psychosis common in AIDS. The higher degree of integration of the archaea into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance.[2] Right hemispheric dominance can lead to acquired immunodeficiency syndrome as has been reported previously from this laboratory. Archaea, viroids and digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype.[34] 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. The increased glycolysis results in the upregulation of mitochondrial PT pore hexokinase resulting in cell proliferation and malignant transformation. The archaeal cholesterol catabolism also generates PAH which can modulate gap junction intercellular communication resulting in cell proliferation and malignant transformation. Archaeal PAH can thus induce neoplastic change. Archaeal cholesterol catabolism can deplete the cells of cholesterol leading onto polyploidy and malignant transformation. There is increased incidence of malignancies is like non-hodgkin's lymphomas and kaposi's sarcoma in AIDS. The lymphocytes depend on glycolysis for their energy needs. The increased glycolysis induced by the Warburg phenotype leads to immune activation. Lactic acid generated by increased glycolysis leads to immune stimulation. Immune stimulation is an association of AIDS syndrome. Cholesterol oxidase activity, increased glycolysis related NADPH oxidase activity and mitochondrial dysfunction generates free radicals important in the pathogenesis of AIDS. Free radicals are used by the HIV virus as messengers and increase retroviral replication and the viral load in the system. 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.[34] The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy needs. The increased cholesterol substrate also leads to increased archaeal growth and digoxin synthesis leading to metabolic channelling to the mevalonate pathway. Hyperdigoxinemia is important in the pathogenesis of AIDS. Digoxin can increase lymphocytic intracellular calcium which leads on to induction of NFKB and immune activation. Digoxin can also induce EGF and other growth factors resulting in oncogenesis. Digoxin can produce increased intracellular calcium related PT pore dysfunction and cell death.[2] The archaeal cholesterol catabolism generated PAH can also produce NMDA excitoxicity and cell death. The archaeal and mevalonate pathway

bacteria cholesterol catabolism can deprive cholesterol from neuronal cell membrane and organelle membranes like mitochondrial, ER and lysosomal membranes producing cellular and organelle dysfunction and death. The Warburg phenotype is also important in neuronal degeneration producing AIDS dementia. The increased glycolysis results in increased generation of the enzyme glyceraldehyde 3 phosphate dehydrogenase (GAPD). GAPD can undergo polyadenylation via free radical activated PARP enzyme. The polyadenylated GAPD can undergo nuclear translocation producing nuclear cell death. All of these contribute to the genesis of neuronal degeneration and AIDS dementia. The AIDS dementia, malignant transformation, immune activation and autoimmune disease which are all part of the HIV syndrome can be related to the archaea and viroids. The cholesterol catabolism by archaea and mevalonate pathway bacteria results in cholesterol depletion from the host which has been described in AIDS. Cholesterol metabolic defects have also been described in creutzfeldt jakob disease. Thus the actinide, viroid and mevalonate pathway bacteria induced metabolic, genetic, immune and neuronal transmission changes can lead onto acquired immunodeficiency syndrome and creutzfeldt jakob disease.

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