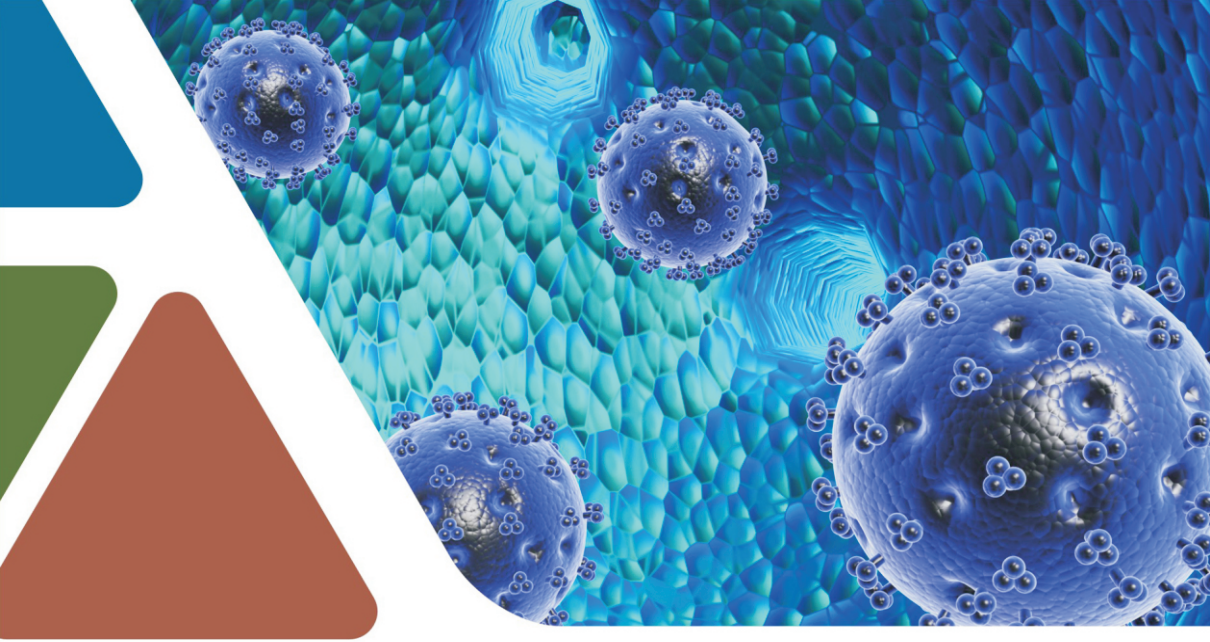

Dietary Fibre Deficiency Syndrome – Evolution of Prion Disease, Retroviral and New Viral Epidemics

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Chapter 1

The Dietary Fibre, Species Evolution and Neuro-Immuno-Genomic-Endocrine Integration

Dietary fibre can affect body and cell function. The original evidence linking dietary fibre and body metabolism in relation to systemic disorders came from the work of Kurup *et al*. where it was shown that the dietary fibre regulates cholesterol metabolism in the body and contributes to the genesis of metabolic syndrome X.[1-7] Dietary fibre deficiency produces predominant small intestinal digestion and dietary fibre excess leads to colonic digestion. Small intestinal digestion in the presence of dietary fibre deficiency leads to alteration in colonic flora and archaeal overgrowth. A high fibre diet produces predominantly colonic digestion and leads to suppression of archaeal growth. The colonic archaea seeps through the gut blood barrier producing archaeal endosymbiosis. Thus small intestinal digestion due to dietary fibre deficiency versus colonic digestion due to dietary fibre excess determines the density of archaea in the colon as well as the endosymbiotic compartment. Dietary fibre deficiency can lead to increased endosymbiotic and colonic archaeal overgrowth. Dietary fibre is the single most important component of the human diet more important than dietary protein, fats, carbohydrates, vitamins and minerals. Dietary fibre is the substrate that determines symbiosis and symbiotic evolution.

Dietary fibre deficiency can lead to increased endosymbiotic as well as colonic archaeal growth leading to recurrent RNA viral epidemics. The endosymbiotic archaea regulates human functions and species type and depends upon the colonic archaea whose density is determined by the fibre intake. The colonic archaeal population density depends upon dietary fibre intake. Populations with low fibre intake have lesser density of colonic archaeal microflora and endosymbiotic archaea. Endosymbiotic archaea contributes to neanderthalisation of the species. Populations consuming a high saturated fat and protein diet with low fibre intake tend to get increased endosymbiotic archaeal growth and are neanderthalised. Populations with high fibre intake up to 80 g/day tend to have reduced archaeal density in the colon and reduced archaeal endosymbiosis contributing to homo

sapienisation of the population. Thus fibre intake regulates the endosymbiotic archaeal density and type of human species.

Dietary fibre can affect brain function. The colonic digestion of dietary fibre by the microflora generates short chain fatty acids. The short chain fatty acid propionate can produce an autistic brain pathology. The short chain fatty acids can bind to GPCR increasing sympathetic activity. The SCFA acetate, propionate and butyrate can be metabolized by the mitochondria generating ATP. The SCFA butyrate is a HDAC inhibitor and modulates genomic transmission.

Butyrate can modulate cognition and increase cognitive function. The acetate is channelled to the glutamate glutamine cycle and modulates neurotransmitter in the synapse. Butyrate can produce histone hyperacetylation and increase BDNF activity. The SCFA can bind to G-protein coupled FFA receptor producing immunosuppression. The short chain fatty acids are anti-inflammatory. Because the SCFA are anti-inflammatory it can modulate insulin resistance. Dietary fibre deficiency can lead to metabolic syndrome and autoimmune disease. Butyrate by producing HDAC inhibition is antioncogenic and inhibits oncogenesis. Butyrate can produce HDAC inhibition and alter protein conformation and folding producing modulation and amelioration of genetic disorders. Butyrate can increase BDNF activity in the brain and produces neuroprotection. Thus a high fibre diet protects against civilisational diseases. Butyrate promotes stem cell transformation and converts fibroblast to pluripotent embryonic stem cells. Thus the fibre derived butyrate is a regenerative molecule. Thus dietary fibre deficiency can lead to cancer, metabolic syndrome, stroke, coronary artery disease, neurodegeneration, genetic disorders, autoimmune diseases and protein folding diseases. Dietary fibre is regulatory substance for the neuronal, immune, genomic and endocrine system.

Dietary fibre can alter the colonic microflora. A high fibre intake suppresses colonic archaeal growth and archaeal endosymbiosis. A high fibre diet suppresses endosymbiotic archaeal growth leading onto homo sapienisation of the species. A high fibre diet leads to increased generation of butyrate and HDAC inhibition leading onto expression of the HERV genes and their reintegration into the genome. The HERV jumping genes contributes to the dynamicity of the genome and is important in the evolution of synaptic connectivity and the homo sapien neocortex. A low fibre diet increases colonic archaeal growth and archaeal endosymbiosis contributing to neanderthalisation of the species and the brain. A low fibre diet and reduced levels of butyrate contributes to modulation of histone acetylation and reduced generation of HERV sequences. This contributes to rigidity of the genome and reduced synaptic connectivity. This leads to cerebral cortical suppression and cerebellar dominance contributing to neanderthalisation of the brain and species. Thus fibre intake in the diet alters symbiotic microflora especially archaeal endosymbiosis and human evolution.

Table 1. *Dietary fibre intake.*

Groups	Fibre content of diet
Homo Sapiens	High fibre 80%
Homo Neanderthalis	Low fibre 70%

*Low fibre < 5 g/day; high fibre > 20 g/day

Table 2. *Dietary fibre intake.*

Groups	Fibre content of diet
Normal	High fibre 80%
Retroviral infection	Low fibre 75%
Recurrent RNA viral infection	Low fibre 65%

*Low fibre < 5 g/day; high fibre > 20 g/day

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Chapter 2

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

Introduction

Dietary fibre deficiency leads to increased endosymbiotic as well as colonic archaeal growth and recurrent RNA viral epidemics/prion disease. The endosymbiotic archaea regulates human functions and species type and depends upon the colonic archaea whose density is determined by the fibre intake. The colonic archaeal population density depends upon dietary fibre intake. Populations with low fibre intake have lesser density of colonic archaeal microflora and endosymbiotic archaea. Endosymbiotic archaea contributes to neanderthalisation of the species. Populations consuming a high saturated fat and protein diet with low fibre intake tend to get increased endosymbiotic archaeal growth and are neanderthalised. Populations with high fibre intake up to 80 g/day tend to have reduced archaeal density in the colon and reduced archaeal endosymbiosis contributing to homo sapienisation of the population. Thus fibre intake regulates the endosymbiotic archaeal density and type of human species.

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 the pathogenesis of acquired immunodeficiency syndrome and Creutzfeldt Jakob's disease.[2] The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered.[5-7] 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's 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 and, (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
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 F420.*

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

Dietary Fibre Deficiency, Endosymbiotic Archaea and Cholesterol Catabolism - Relation to Prion Disease and Retroviral Infection

Dietary fibre deficiency leads to increased endosymbiotic as well as colonic archaeal growth. There was increase in cytochrome F420 indicating archaeal growth in acquired immunodeficiency syndrome and Creutzfeldt Jakob's 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 noncoding 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 signalling 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.

Dietary Fibre Deficiency, Endosymbiotic Archaea and Genomic Change - Relation to Prion Disease and Retroviral Infection

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 multicellular eukaryote. Pollution is induced by the primitive nanoarchaea and mevalonate pathway

bacteria synthesized PAH and methane leading on to redox stress. Redox stress leads to sodium potassium ATPase inhibition, inward movement of plasma membrane cholesterol, defective SREBP sensing, increased cholesterol synthesis and nanoarchaeal/mevalonate pathway bacterial growth.[29] Redox stress leads on to viroidal and archaeal multiplication. Redox stress can also lead to HERV reverse transcriptase and integrase expression. The noncoding DNA is formed of integrating RNA viroidal complementary DNA and archaea with the integration going on as a continuing event. The archaeal pox like dsDNA virus forms evolutionarily the nucleus. The integrated viroidal, archaeal and mevalonate pathway bacterial sequences can undergo vertical transmission and can exist as genomic parasites. The genomic integrated archaea, mevalonate pathway bacteria and viroids form a genomic reserve of bacteria and viruses which can recombine with human and eukaryotic genes producing bacterial and viral speciation. Bacteria and viruses have been related to the pathogenesis of acquired immunodeficiency syndrome and Creutzfeldt Jakob's 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's 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.

Dietary Fibre Deficiency, Endosymbiotic Archaea and Neuro-Endocrine-Immune Dysregulation - Relation to Prion Disease and Retroviral Infection

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 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's 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's disease.

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Chapter 3

Endosymbiotic Archaeal Generated RNA Viroids Can Regulate Cell Function and Contribute to Disease State – Role in Viral Speciation

Introduction

Dietary fibre deficiency leads to increased endosymbiotic as well as colonic archaeal growth and recurrent viral infection. The endosymbiotic archaea regulates human functions and species type and depends upon the colonic archaea whose density is determined by the fibre intake. The colonic archaeal population density depends upon dietary fibre intake. Populations with low fibre intake have lesser density of colonic archaeal microflora and endosymbiotic archaea. Endosymbiotic archaea contributes to neanderthalisation of the species. Populations consuming a high saturated fat and protein diet with low fibre intake tend to get increased endosymbiotic archaeal growth and are neanderthalised. Populations with high fibre intake up to 80 g/day tend to have reduced archaeal density in the colon and reduced archaeal endosymbiosis contributing to homo sapienisation of the population. Thus fibre intake regulates the endosymbiotic archaeal density and type of human species.

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, 2] Organisms like phytoplasmas and viroids have also been demonstrated to play a role in the etiology of these diseases.[3, 4] RNA viroids could contribute to the pathogenesis of schizophrenia, malignancy, metabolic syndrome X, autoimmune disease and neuronal degeneration.[2] The possibility of generation of RNA viroids by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered.[5-8] An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described.[6] The role of RNA viroids generated by actinidic archaea in regulation of body functions and the pathogenesis of human disease is discussed.

Materials and Methods

Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The following groups were included in the study: - 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's 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 and, (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 and free DNA.[11-14] Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). The statistical analysis was done by ANOVA.

Results

The parameters checked as indicated above were: - cytochrome F420, free RNA and free DNA. Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a

decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-2 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

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

Group	**CYT F420 % (Increase with Rutile)**		**CYT F420 % (Decrease with Doxy+Cipro)**	
	Mean	**± SD**	**Mean**	**± SD**
Normal	4.48	0.15	18.24	0.66
Schizo	23.24	2.01	58.72	7.08
Seizure	23.46	1.87	59.27	8.86
AD	23.12	2.00	56.90	6.94
MS	22.12	1.81	61.33	9.82
NHL	22.79	2.13	55.90	7.29
DM	22.59	1.86	57.05	8.45
AIDS	22.29	1.66	59.02	7.50
CJD	22.06	1.61	57.81	6.04
Autism	21.68	1.90	57.93	9.64
EMF	22.70	1.87	60.46	8.06
F value	306.749		130.054	
P value	< 0.001		< 0.001	

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

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy+Cipro)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
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		356.621		427.828		654.453	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Discussion

Dietary Fibre Deficiency, Endosymbiotic Archaea and Cholesterol Catabolism

Dietary fibre deficiency leads to increased endosymbiotic as well as colonic archaeal growth. There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source.[15, 16] The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities.[17, 18] The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms.[19]

Dietary Fibre Deficiency, Endosymbiotic Archaea and Genomic Dysfunction - Relation to Viral Speciation

There was an increase in free RNA indicating self replicating RNA viroids and free DNA indicating generation of viroid complementary DNA strands by archaeal reverse transcriptase activity. The actinides modulate RNA folding and catalyse its ribozymal action. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities.[20] Archaea induced immune activation and redox stress can produce histone deacetylase inhibition resulting in endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the RNA viroidal complementary DNA into the noncoding region of eukaryotic noncoding DNA using HERV integrase as has been described for borna and ebola viruses.[21] The noncoding DNA is lengthened by integrating RNA viroidal complementary DNA with the integration going on as a continuing event. The archaea genome can also get integrated into human genome using integrase as has been described for trypanosomes.[22] The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites.[21, 22] This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters.[23] The viroidal complementary DNA can function as jumping genes producing a dynamic genome important in storage of synaptic information, HLA gene expression and developmental gene expression. The RNA viroids can regulate mRNA function by RNA interference.[20] The phenomena of RNA interference can modulate T cell and B cell function, insulin signalling lipid metabolism, cell growth and differentiation, apoptosis, neuronal transmission and euchromatin/heterochromatin expression.

The RNA viroids and its complementary DNA developed into cholesterol enveloped RNA and DNA viruses like herpes, retrovirus, influenza virus, borna virus, cytomegalo virus and ebstein barr virus by recombining with archaeal,

eukaryotic and human genes resulting in viral speciation.[24-26] The RNA viroids can also recombine with endogenous commensal RNA and DNA viruses producing speciation. Viral species are ill defined and fuzzy with all of them forming one common genetic pool with frequent horizontal gene transfer and recombination. Thus the multi and unicellular eukaryote with its genes serves the purpose of viral speciation.

Dietary Fibre Deficiency, Endosymbiotic Archaea and Genomic Change - Relation to Bacterial Speciation

The multicellular eukaryotes are like archaeal biofilms. The archaea with a mevalonate pathway uses the extracellular RNA viroids for quorum sensing and in the generation of symbiotic biofilm like structures which develop into multicellular eukaryotes.[27, 28] The endosymbiotic archaea and bacteria with mevalonate pathway still uses the RNA viroids for the regulation of multicellular eukaryote. Pollution is induced by the primitive nanoarchaea and mevalonate pathway bacteria synthesized PAH and methane leading on to redox stress. Redox stress leads to sodium potassium ATPase inhibition, inward movement of plasma membrane cholesterol, defective SREBP sensing, increased cholesterol synthesis and nanoarchaeal/mevalonate pathway bacterial growth.[29] Redox stress leads on to viroidal and archaeal multiplication. Redox stress can also lead to HERV reverse transcriptase and integrase expression. The noncoding DNA is formed of integrating RNA viroidal complementary DNA and archaea with the integration going on as a continuing event. The archaeal pox like dsDNA virus forms evolutionarily the nucleus. The integrated viroidal, archaeal and mevalonate pathway bacterial sequences can undergo vertical transmission and can exist as genomic parasites. The genomic integrated archaea, mevalonate pathway bacteria and viroids form a genomic reserve of bacteria and viruses which can recombine with human and eukaryotic genes

producing bacterial and viral speciation. The change in the length and grammar of the noncoding region produces eukaryotic speciation and individuality.[30] The integration of nanoarchaea, mevalonate pathway prokaryotes and viroids in to the eukaryotic and human genome produces a chimera which can multiply producing biofilm like multicellular structures having a mixed archaeal, viroidal, prokaryotic and eukaryotic characters which is a regression from the multicellular eukaryotic tissue. This results in a new neuronal, metabolic, immune and tissue phenotype leading to human disease.

Dietary Fibre Deficiency, Endosymbiotic Archaea and Defective Neuro-Immuno-Endocrine-Genomic Integration - Relation to Bacterial and Viral Speciation and Systemic Disease

The archaea and viroids can regulate the nervous system including the NMDA/GABA thalamo-cortico-thalamic pathway mediating conscious perception.[2, 31] NMDA/GABA receptors can be modulated by viroid induced RNA interference.[2] The dipolar viroids combined with actinides 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, 31] The viroids can regulate limbic lobe transmission by RNA viroid mediated RNA interference modulating norepinephrine, dopamine, serotonin and acetyl choline receptors.[18] The higher degree of integration of the archaea and viroids into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance.[2] The viroid RNA interference mediated altered monoamine and NMDA transmission contributes to the pathogenesis of schizophrenia and autism. Archaea and RNA viroid can bind the TLR receptor induce NFKB producing immune activation

and cytokine TNF alpha secretion.[2, 32] The archaea and viroid induced chronic immune activation and generation of superantigens can lead on to autoimmune disease. Archaea and viroids can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype.[33] The increased glycolytic hexokinase activity, decrease in blood ATP, leakage of cytochrome C, increase in serum pyruvate and decrease in acetyl CoA indicates the generation of the Warburg phenotype. There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics and metabolic syndrome. The archaea and viroid generated cytokines can lead to TNF alpha induced insulin resistance and metabolic syndrome X. The accumulated pyruvate enters the GABA shunt pathway and is converted to citrate which is acted upon by citrate lyase and converted to acetyl CoA, used for cholesterol synthesis.[33] The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy needs. The increased cholesterol substrate leads to increased archaeal growth and digoxin synthesis leading to metabolic channelling to the mevalonate pathway.[34] The archaea and viroid induced monocyte activation and Warburg phenotype induced increased cholesterol synthesis leads to atherogenesis. Viroid induced RNA interference can modulate the mRNAs concerned with insulin receptor function and lipid metabolism contributing to metabolic syndrome X. The Warburg phenotype induced increased mitochondrial PT pore hexokinase can lead on to malignant transformation. Viroid induced RNA interference can modulate oncogenes producing malignant transformation. The viroid induced RNA interference can modulate the mRNA concerned with the death receptor pathway producing apoptosis and neuronal 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.

Thus the actinidic archaea generated RNA viroids can regulate cell function and produce neuro-immuno-genetic-endocrine-metabolic integration. The RNA viroids and their complementary DNA can serve the purpose of viral speciation. The RNA viroids also contributes to the pathogenesis of schizophrenia, malignancy, metabolic syndrome X, autoimmune disease and neuronal degeneration.

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Chapter 4

The Extinction of Homo Sapiens and Symbiotic Neanderthalisation - Relation to Archaeal Mediated RNA Viroids and Amyloidosis

Introduction

The endosymbiotic archaea regulates human functions and species type and depends upon the colonic archaea whose density is determined by the fibre intake. The colonic archaeal population density depends upon dietary fibre intake. Populations with low fibre intake have lesser density of colonic archaeal microflora and endosymbiotic archaea. Endosymbiotic archaea contributes to neanderthalisation of the species. Populations consuming a high saturated fat and protein diet with low fibre intake tend to get increased endosymbiotic archaeal growth and are neanderthalised. Populations with high fibre intake up to 80 g/day tend to have reduced archaeal density in the colon and reduced archaeal endosymbiosis contributing to homo sapienisation of the population. Thus fibre intake regulates the endosymbiotic archaeal density and type of human species.

Prion proteins have been implicated in systemic disorders like neurodegenerations, cancer and metabolic syndrome. 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 proteins like behaviour is also seen in the tumour suppressor P_{53} protein in cancer and the islet cell associated amyloid in diabetes mellitus. 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, 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 metabolic syndrome,

neurodegenerations, cancer, autoimmune disease, schizophrenia, autism and CJD. The RNA viroids can bind with normal proteins with prion like domains eg, superoxide dismutase and produce a ribonucleoprotein resulting in prion phenomena and amyloidogenesis. The actinidic archaeal growth results in increased digoxin synthesis and phenotypic conversion of homo sapiens to homo Neanderthals as reported earlier. The increased actinidic archaeal growth is due to global warming and this results in neanderthalisation. Homo neanderthalis tend to have more of civilisational diseases like metabolic syndrome, neurodegenerations, cancer, autoimmune disease, schizophrenia, autism and CJD. 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: - 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's 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+cerium 0.1 mg/ml and, (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 CJD and other disease groups indicating increased archaeal growth. There was also an increase in free RNA indicating self replicating RNA viroids in CJD and other disease groups. The RNA viroid generation was catalysed by actinides. The RNA viroids can bind with proteins having prion like domains forming ribonucleoproteins. These ribonucleoproteins can give an abnormal conformation to the protein resulting in generation of abnormal prions. The abnormal prions can act as a template to convert normal proteins with normal configuration to abnormal conformation. This can result in amyloidogenesis. The abnormal configured proteins will resist lysosomal digestion and accumulate as amyloid.

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
Schizo	23.24	2.01	58.72	7.08
Seizure	23.46	1.87	59.27	8.86
AD	23.12	2.00	56.90	6.94
MS	22.12	1.81	61.33	9.82
NHL	22.79	2.13	55.90	7.29
DM	22.59	1.86	57.05	8.45
AIDS	22.29	1.66	59.02	7.50
CJD	22.06	1.61	57.81	6.04
Autism	21.68	1.90	57.93	9.64
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
Schizo	23.59	1.83	65.69	3.94
Seizure	23.08	1.87	65.09	3.48
AD	23.29	1.92	65.39	3.95
MS	23.29	1.98	67.46	3.96
NHL	23.78	1.20	66.90	4.10
DM	23.33	1.86	66.46	3.65
AIDS	23.32	1.74	65.67	4.16
CJD	23.11	1.52	66.68	3.97
Autism	23.33	1.35	66.83	3.27
F value	427.828		654.453	
P value	< 0.001		< 0.001	

Discussion

Dietary Fibre Deficiency, Endosymbiotic Archaea and Amyloidogenesis

Dietary fibre deficiency leads to increased endosymbiotic as well as colonic archaeal growth. There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source. The archaeal origin of the self replicating RNA was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by cerium induced increase in enzyme activities. There was an increase in free RNA indicating self replicating RNA viroids. The actinides modulate RNA folding and catalyse its ribozymal action. Digoxin can cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities. The RNA viroids can bind with proteins having prion like domains forming ribonucleoproteins. These ribonucleoproteins can give an abnormal conformation to the protein resulting in generation of abnormal prions. The abnormal prions can act as a template to convert normal proteins with normal configuration to abnormal conformation. This can result in amyloidogenesis. The abnormal configured proteins will resist lysosomal digestion and accumulate as amyloid.

Amyloidogenesis has been implicated in systemic disorders. 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 proteins like behaviour is also

seen in the tumour suppressor P_{53} protein in cancer and the islet cell associated amyloid in diabetes mellitus. Prion diseases are conformational diseases.

Dietary Fibre Deficiency, Endosymbiotic Archaea and RNA Viroids - Relation to Amyloidogenesis

The RNA viroids generated from actinidic archaea can bind to proteins with prion like domains resulting in generation of ribonucleoproteins. Ribonucleoproteins with abnormal conformation can act as a template for normal proteins with prion like domains to change to abnormal conformation. This results in generation of prion proteins with abnormal conformation resisting lysosomal digestion and generating amyloid. These systemic diseases are due to actinidic archaeal generated RNA viroid induced prion protein generation and amyloidogenesis. Prion proteins have been implicated in systemic disorders like neurodegenerations, cancer and metabolic syndrome. 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 proteins like behaviour is also seen in the tumour suppressor P_{53} protein in cancer and the islet cell associated amyloid in diabetes mellitus. The present study shows that the same prion protein mechanism can operate in schizophrenia, autism and autoimmune diseases. 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, cancer, metabolic syndrome, autoimmune disease and neuropsychiatric diseases.

Dietary Fibre Deficiency, Endosymbiotic Archaea and Porphyrionogenesis - Relation to Amyloidogenesis

The archaeal porphyrins can modulate amyloid formation. The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide. The pyruvate gets converted to glutamate and ammonia by the GABA shunt pathway. The pyruvate is converted to glutamate by serum glutamate pyruvate transaminase. The glutamate gets acted upon by glutamate dehydrogenase to generate alpha ketoglutarate and ammonia. Alanine is most commonly produced by the reductive amination of pyruvate via alanine transaminase. This reversible reaction involves the interconversion of alanine and pyruvate, coupled to the interconversion of alpha-ketoglutarate (2-oxoglutarate) and glutamate. Alanine can contribute to glycine. Glutamate is acted upon by Glutamic acid decarboxylase to generate GABA. GABA is converted to succinic semialdehyde by GABA transaminase. Succinic semialdehyde is converted to succinic acid by succinic semialdehyde dehydrogenase. Glycine combines with succinyl CoA to generate delta aminolevulinic acid catalysed by the enzyme ALA synthase. There was upregulated archaeal porphyrin synthesis in the patient population which was archaeal in origin as indicated by actinide catalysis of the reactions. The cholesterol oxidase pathway generated pyruvate which entered the GABA shunt pathway. This resulted in synthesis of succinate and glycine which are substrates for ALA synthase. Glycine and succinyl CoA are the substrates for ALA synthesis. Porphyrin and ALA inhibits sodium potassium ATPase. This increases cholesterol synthesis by acting upon intracellular SREBP. The cholesterol is metabolized to pyruvate and then the GABA shunt pathway for ultimate use in porphyrin synthesis. The porphyrins can self organize and self replicate into macromolecular arrays. The porphyrin arrays behave like an autonomous organism and can have intramolecular electron transport generating

ATP. The porphyrin macroarrays can store information and can have quantal perception. The porphyrin macroarrays serves the purpose of archaeal energetics and sensory perception. Protoporphyrine binds to the peripheral benzodiazepine receptor regulating steroid and digoxin synthesis. Increased porphyrin metabolites can contribute to hyperdigoxinemia. Digoxin can modulate the neuro-immuno-endocrine system.

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 systemic diseases like neurodegenerations, cancer, metabolic syndrome, autoimmune disease and neuropsychiatric diseases. The widespread incidence of these systemic diseases leads to extinction of the neanderthalised species.

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Chapter 5

The Origin of Retroviral Resistance and Emerging Viral Pandemics - The Crossing of Species Barrier and New Viruses

Introduction

The endosymbiotic archaea regulates human functions and species type and depends upon the colonic archaea whose density is determined by the fibre intake. The colonic archaeal population density depends upon dietary fibre intake. Populations with low fibre intake have lesser density of colonic archaeal microflora and endosymbiotic archaea. Endosymbiotic archaea contributes to neanderthalisation of the species. Populations consuming a high saturated fat and protein diet with low fibre intake tend to get increased endosymbiotic archaeal growth and are neanderthalised. Populations with high fibre intake up to 80 g/day tend to have reduced archaeal density in the colon and reduced archaeal endosymbiosis contributing to homo sapienisation of the population. Thus fibre intake regulates the endosymbiotic archaeal density and type of human species.

Studies from our laboratory have shown that global warming and the low level EMF pollution results in increased endosymbiotic archaeal growth. The archaea can produce methanogenesis from hydrogen and carbon dioxide as well as from acetate. The human body methanogenesis can result in more global warming. Methane has got a short term action but its global warming potential is 29 times that of carbon dioxide. Thus the human endosymbiotic archaeal overgrowth is the principal cause of global warming. Global warming is initially triggered by carbon dioxide and EMF pollution produced by homo sapien industrialization. It is carried forward by human endosymbiotic archaeal overgrowth and methanogenesis. The archaea can induce stem cell conversion and neanderthalisation of the human species. The archaea catabolises cholesterol generating digoxin which can modulate RNA editing and magnesium deficiency resulting in reverse transcriptase inhibition. The archaeal cholesterol catabolism can deplete the membrane rafts of the CD4 cell of cholesterol impeding the entry of the retrovirus into the cell. The archaea can produce permanent immune

activation producing resistance to viral and bacterial infection. The archaeal cholesterol catabolism depletes tissue cholesterol producing vitamin D deficiency and immune activation. Thus archaeal overgrowth results in retroviral resistance and generation of the Neanderthal phenotype. The endosymbiotic archaea can secrete virus like RNA and DNA particles. The endosymbiotic archaea can induce uncoupling proteins inhibiting mitochondrial oxidative phosphorylation and generating ROS. The endosymbiotic archaeal magnetite can generate low level of EMF. The low level of EMF and ROS are genotoxic and produce breakages in hotspots of chromosome. It can also trigger rearrangements in hotspots of chromosome inhabited by retroviral and non-retroviral elements producing their expression. The archaeal secreted DNA and RNA viroids can recombine with the expressed retroviral, non-retroviral elements and other genomic segments of the human chromosome generating new RNA and DNA viruses. Thus the neanderthalised humans can serve as an origin for new RNA and DNA viruses as well as mutated retroviruses. The endosymbiotic archaea converts the Neanderthal cells to stem cells. The stem cells are resistant to immune attack. The stem cells can serve as a reservoir for this new RNA and DNA viruses. The stem cells and archaeal cells can also serve as a reservoir for viruses and bacteria belonging to other plants and animals. This helps to generate the species barrier jump in noted in recent emerging viral and bacterial infections. Thus the endosymbiotic archaeal growth produces neanderthalised version of homo sapiens which are retroviral resistant and resistant to other viral and bacterial infection consequent to immune activation and digoxin induced RNA editing. The endosymbiotic archaeal overgrowth mediated neanderthalised version of homo sapiens generates new mutated RNA and DNA viruses as well as retroviruses at the same time being resistant to them as in the case of the species bat. The homo sapiens do not have the Neanderthal mechanisms of immune activation as their archaeal load is meagre. They serve as fodder for infection

from Neanderthal generated viruses and bacteria and suffer eventual extinction. This paper studied the archaeal status in patients with recurrent viral infections and retroviral infections. The generation of RNA and DNA viroids from archaea was also studied.[1-17]

Materials and Methods

Blood samples were drawn from normal population, Neanderthal phenotype, retroviral infection and recurrent viral infection. 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 and, (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 and free DNA. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm).

Results

Plasma of Neanderthal phenotype 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 retroviral patients and those with recurrent viral infections showed similar results but the extent of increase was insignificant. 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 Neanderthal phenotype sera as compared to patients with retroviral infection and recurrent viral infection. The results are expressed in tables 1-2 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

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

Group	CYT F420 % (Increase with Cerium)		CYT F420 % (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD
Retroviral & frequent viral infection	4.48	0.15	18.24	0.66
Neanderthal phenotype	23.46	1.87	59.27	8.86
F value	306.749		130.054	
P value	< 0.001		< 0.001	

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

Group	DNA % change (Increase with Cerium)		DNA % change (Decrease with Doxy+Cipro)		RNA % change (Increase with Cerium)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Retroviral & frequent viral infection	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
Neanderthal phenotype	23.40	1.51	63.68	4.66	23.08	1.87	65.09	3.48
F value	337.577		356.621		427.828		654.453	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Discussion

Dietary Fibre Deficiency, Endosymbiotic Archaea and Retroviral Resistance

Dietary fibre deficiency leads to increased endosymbiotic as well as colonic archaeal growth. The archaeal symbiosis results in cholesterol catabolism and synthesis of digoxin. Digoxin has an APOBEC-like action producing RNA

editing. This mutates the HIV virus inhibiting its replication. Digoxin is a membrane sodium potassium ATPase inhibitor. It produces magnesium deficiency intracellularly. Magnesium can inhibit reverse transcriptase activity inhibiting HIV replication. Endosymbiotic archaea can induce porphyrin synthesis. Porphyrin can combine with HIV virus inactivating it. The endosymbiotic archaea produces cholesterol catabolism and uses cholesterol as an energy source. This results in modulation of membrane rafts of the CD4 receptor resulting in retroviral resistance. The archaeal cholesterol catabolism produces cholesterol depletion and vitamin D deficiency. This produces immune activation. The endosymbiotic archaeal growth as such produces permanent immune activation resulting in resistance to viral infections. This has been demonstrated in bacteria like *mycobacterium leprae*. The immune genes are always turned on inhibiting retroviral and other viral replication. The endosymbiotic archaeal growth results in turning in of uncoupling proteins transferring human somatic cells to the Warburg phenotype and stem cell type. Stem cells have the energetics obtained from glycolysis and not from mitochondrial oxidative phosphorylation. Stem cells are resistant to retroviral infection and other viral infection. Thus endosymbiotic archaeal growth can inhibit HIV replication and produce HIV resistance.[1-17]

Dietary Fibre Deficiency, Endosymbiotic Archaea and Neanderthalisation - Relation to Retroviral Resistance

Endosymbiotic archaeal growth produces neanderthalisation of the human species. The homo neanderthalis can serve as a reservoir for viral infections at the same time being resistant to it. The homo neanderthalis has the stem cell phenotype which can serve as a reservoir for bacterial and viral infection. This has been demonstrated in the case of mycobacterium tuberculosis which induces stem cell transformation and survives within the stem cell resisting immune

onslaught. This protective mechanism is not available for the homo sapien species and they tend to succumb to viral infections arising from the homo neanderthalis reservoir.[1-17]

The homo neanderthalis has archaeal induced induction of uncoupling proteins producing mitochondrial oxidative phosphorylation inhibition and dominant glycolytic energetics. This results in conversion to a stem cell phenotype. The high metabolic rate results in a fever response which turns on the immune system resulting in permanent immune activation. The high temperatures also damage the cell producing a system of high efficiency DNA repair. This results in permanent resistance to viral infections consequent to continuous immune activation and high efficiency DNA repair. The increased archaeal growth in homo neanderthalis produces uncoupling proteins and stem cell conversion making it also resistant to viral infections. This produces a system of viral reservoir in homo neanderthalis like bats which serves as a reservoir for rabies virus, Ebola virus and SARS virus. The bats also have archaeal endosymbionts. Archaeal endosymbionts have been demonstrated in the bat guano pile.[1-17]

Dietary Fibre Deficiency, Endosymbiotic Archaea and Porphyrinogenesis - Relation to Genomic Instability and Generation of New Viral Species

The archaeal magnetite produces increased level of low level EMF in the homo neanderthalis producing genomic instability. The human genome contains viral sequences like the ebola virus, retro virus and the borna virus. Owing to the archaeal magnetite induced low level EMF mediated genomic instability the viral elements in the human genome gets expressed. The archaeal magnetite induced low level EMF as well as archaea itself produces permanent continuous immune activation results in protection against viral infections. Thus in the homo

neanderthalis the viral elements in the genome functioning as genomic parasites gets expressed and the homo neanderthalis serves as a reservoir for viruses akin to bats which are also part of the primate kingdom. The archaea in the homo neanderthalis secretes DNA and RNA viroids which can self replicate on porphyrin templates. Virus-like particles and extracellular DNA are produced by the hyperthermophilic archaea-thermococcales. The RNA viroids can get converted to DNA by HERV reverse transcriptase and get integrated into the neanderthalic genome by integrase. The DNA viroids secreted by the archaea can also gets integrated into the human genome by integrase. Thus the archaeal RNA and DNA viroids which are of great diversity get integrated into the human genome by the action of integrase and HERV reverse transcriptase.[1-17]

The genomic instability of the neanderthalic genome consequent to low level EMF generated by archaeal magnetite as well as archaeal porphyrins intercalating with human DNA can result in expression of viral elements of the human genome. RNA polyribonucleotides from chromosome 22q11.2 ALU sequences have been demonstrated in the sera of patients with Gulf war syndrome and multiple myloma. The exposure to genotoxic substances and low level EMF results in activation of retrotransposon ALU elements leading to the unique RNA segments in the serum. The RNA polyribonucleotides have the proteolipid cover which resists digestion by enzymes. The SARS virus spike protein is expressed consequent to complex genetic rearrangement of segmental hotspots of chromosome-7 due to catastrophic environmental EMF exposure. Humans and animals exposed the nuclear or chemical weapons or continuous low level EMF radiation produces new regulatory gene expression which are then transcribed as non-viral RNA microvissicules covered by proteolipid membranes. Low level of EMF and genotoxic agents leads to gene rearrangement of ALU sequences with generation of RNA polyribonucleotides

covered by proteiolipid vesicles. The SARS virus is supposed to be due to complex reshuffling of hotspots of chromosome 7.[1-17]

The archaea produces uncoupling of the mitochondrial oxidative phosphorylation of the somatic cells. The archaeal magnetite produces expression of low level of EMF. The reactive oxygen species produced by uncoupling of mitochondrial oxidative phosphorylation and low EMF produced by archaeal magnetite are genotoxic and produces complex rearrangement of the Neanderthal genome, breakage of hotspots in the chromosome which are extremely fragile producing expression of RNA polyribonucleotides which can get converted to DNA polyribonucleotides by the enzyme HERV reverse transcriptase. The RNA and DNA polyribonucleotides packaged in proteolipid vesicles can mimic RNA and DNA viruses. The junk DNA of humans are constituted by HERV sequences and non-retroviral RNA viruses like Ebola and borna viruses. They are genomic parasites. The neanderthalic cell has increased production of ROS consequent to archaeal induced uncoupling. The archaeal magnetite induced EMF as well as archaea induced uncoupling generated ROS are genotoxic. The exposure to ROS and low level EMF can produce rearrangement of junk DNA producing new type of RNA viruses which can get expressed. The viral-retroviral and non-retroviral elements of the human genome as well as human genomic sequences per se which are expressed can recombine with the archaeal DNA and RNA viroids producing new mutated dangerous viruses both of the RNA and DNA type in the homo neanderthalis. The homo neanderthalis have uncoupled oxidative phosphorylation and more of ROS production. The ROS serves as messengers modulating viral replication. Thus there is genomic instability inducing expression of the viral elements in the neanderthalic genome, archaeal expression of DNA and RNA viroids, recombination of DNA and RNA archaeal viroids with neanderthalic genomic viral elements which are expressed and ROS induced multiplication of newly mutated virus.[1-17]

Dietary Fibre Deficiency, Endosymbiotic Archaea and Neanderthalisation - Relation to New Viral Infection and Extinction of Homo Sapiens

The homo neanderthalis themselves are resistant to these viruses and serve as a reservoir for them like their primate brother the bat. The homo sapiens have less endosymbiotic archaeal symbiosis and have no uncoupling protein induction resulting in maintenance of their mature somatic cells as such. The homo sapien cell has dominant mitochondrial oxidative phosphorylation metabolism generating less of ROS. The homo sapiens are immunosuppressed. The homo sapiens are not permanently immune activated producing viral resistance. They don't have the stem cell phenotype. They don't have dominant archaeal mediated cholesterol catabolism modulating viral receptors. The homo sapiens don't have digoxin synthesis inhibiting RNA editing and viral replication. The homo sapiens are sitting ducks for viral infections generated by homo neanderthalis which infects them and kills them. The homo neanderthalis which generated the viruses in the first place are resistant to the viral infections. The homo sapien species gets exterminated from the viral infection generated from homo neanderthalis. The homo neanderthalis species uses viral infection as a mechanism to eliminate the homo sapiens and produce species dominance.[1-17]

Dietary Fibre Deficiency, Endosymbiotic Archaea and Homo Sapien Extinctus

The homo neanderthalis has archaea as endosymbionts. The archaea behaves like stem cells and can induce conversion of somatic cells to stem cells. The stem cells and archaeal cells can serve as reservoirs of other species virus and bacteria like plant and animal viruses and bacteria. The plant and animal viruses and bacteria can thrive in the somatic stem cells and archaeal cells as they escape immune detection. The Neanderthals tissue system can be compared to an archaeal/stem cell colony or network which serves as a reservoir for other

animal and plant species bacteria and viruses as well as a generating centre for new RNA and DNA viruses. The RNA and DNA viruses are created by recombination between expressed genetically rearranged bits of the human chromosome and virus like DNA and RNA particles secreted by the archaea. This paves way for the generation of unlimited number of new RNA and DNA viruses as well as produce conditions for viruses and bacteria to cross the species barrier. This is evidenced by the SARS virus, the nipah virus and hendra virus crossing species. The algal virus has been reported to infect human brains producing cognitive dysfunction. The generation of new RNA and DNA viruses and the creation of a stem cell/archaeal reservoir for other species bacteria and viruses, the Neanderthal resistance to infections by viruses and bacteria and the Neanderthals serving as a reservoir for infection results in widespread pandemic in the homo sapien population in Africa and their eventual wipeout.[1-17]

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Chapter 6

Endosymbiotic Actinidic Archaea and Viroids-A Model for Abiogenesis and Viral, Prokaryote, Eukaryotic, Primate and Human Evolution

Introduction

The endosymbiotic archaea regulates human functions and species type and depends upon the colonic archaea whose density is determined by the fibre intake. The colonic archaeal population density depends upon dietary fibre intake. Populations with low fibre intake have lesser density of colonic archaeal microflora and endosymbiotic archaea. Endosymbiotic archaea contributes to neanderthalisation of the species. Populations consuming a high saturated fat and protein diet with low fibre intake tend to get increased endosymbiotic archaeal growth and are neanderthalised. Populations with high fibre intake up to 80 g/day tend to have reduced archaeal density in the colon and reduced archaeal endosymbiosis contributing to homo sapienisation of the population. Thus fibre intake regulates the endosymbiotic archaeal density and type of human species.

A hypothesis regarding endosymbiotic actinidic archaea as having evolved from an early isoprenoid organisms by abiogenesis is presented in this paper. An actinidc archaea/viroid mediated model of prokaryote, viral, eukaryotic, primate and human evolution is discussed. 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, 2] Organisms like phytoplasmas and viroids have also been demonstrated to play a role in the etiology of these diseases.[3, 4] Actinidic archaea has been related to the pathogenesis of schizophrenia, malignancy, metabolic syndrome X, autoimmune disease and neuronal degeneration.[2] Actinidic archaea have a mevalonate pathway and cholesterol catabolism.[5-7] 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] Metal actinides in beach sands have been postulated to play a role in abiogenesis.[6] Actinide mineral like rutile, monazite and illmenite by surface metabolism would have contributed to abiogenesis.[9] 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. The actinidic archaea and viroids would have evolved from the primitive isoprenoid organism. The origin of viruses, prokaryotes, eukaryotes, primates and humans from the initial isoprenoid organism derived actinidic archaea is postulated.

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: - 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's 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 and, (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, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin,

pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids.[11-14] 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 cytochrome F420 and muramic acid.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)		Muramic acid % change (Increase with Rutile)		Muramic acid % 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		130.054		391.318		257.996	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy+Cipro)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
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		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 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		199.553		449.503		673.081	
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+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		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+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		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+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		171.228		372.716		556.411	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

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

Group	PAH % (Increase with Rutile)		PAH % (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		680.284		348.867		364.999	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Discussion

Dietary Fibre Deficiency, Endosymbiotic Archaea and Cholesterol Catabolism - Relation to Speciation of Virus and Bacteria

Dietary fibre deficiency leads to increased endosymbiotic as well as colonic archaeal growth. There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source.[15, 16] The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities.[17] 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.[16] 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.[18] 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.[19]

The metal actinides provide radiolytic energy, catalysis for oligomer formation and provide a coordinating ion for metalloenzymes all important in abiogenesis.[6] 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.[8, 9, 20] Cholesterol by radiolysis by actinides would have formed PAH generating PAH aromatic organism.[8] 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 an evolutionary advantage. The symbiosis of archaea with gram negative organism generated the eukaryotic cell.[21] 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.

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. 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 noncoding DNA using HERV integrase as has been described for borna and ebola viruses.[21] The noncoding DNA is lengthened by integrating RNA viroidal complementary DNA with the integration going on as a continuing event. The archaea genome can also get integrated into human genome using integrase as has been described for trypanosomes. The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites. This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters. The viroidal complementary DNA can function as jumping genes producing a dynamic genome.[22-24]

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. The bacteria and archaea with mevalonate pathway and cholesterol catabolism had an evolutionarily advantage and constitutes the isoprenoidal clade organism. The archaea evolved into mevalonate pathway gram positive and gram negative isoprenoid clade organism through horizontal gene transfer of viroidal and virus genes. The isoprenoidal clade prokaryotes develop into other groups of

prokaryotes via viroidal/virus as well as eukaryotic horizontal gene transfer producing bacterial speciation.[25-27]

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. The endosymbiotic archaea and bacteria with mevalonate pathway still uses the RNA viroids and DNA viroids for the regulation of multicellular eukaryote.[28-31]

Pollution and Evolutionary Innovation

Pollution is a major inducer of evolutionary innovation. 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. Redox stress leads on to viroidal and archaeal multiplication. Redox stress can also lead to HERV reverse transcriptase and integrase expression. The noncoding DNA is formed of integrating RNA viroidal complementary DNA and archaea with the

integration going on as a continuing event. The archaeal pox like dsDNA virus forms evolutionarily the nucleus. The integrated viroidal, archaeal and mevalonate pathway bacterial sequences can undergo vertical transmission and can exist as genomic parasites. The genomic integrated archaea, mevalonate pathway bacteria and viroids form a genomic reserve of bacteria and viruses which can recombine with human and eukaryotic genes producing bacterial and viral speciation. The change in the length and grammar of the noncoding region produces eukaryotic speciation and individuality. The integration of nanoarchaea, mevalonate pathway prokaryotes and viroids in to the eukaryotic and human genome produces a chimera which can multiply producing biofilm like multicellular structures having a mixed archaeal, viroidal, prokaryotic and eukaryotic characters which is a regression from the multicellular eukaryotic tissue. This results in a new neuronal, metabolic, immune and tissue phenotype leading to human disease.[30-32]

Pollution would have been a major factor in eukaryotic speciation and primate/hominid evolution. The change in the length and grammar of the noncoding region produces eukaryotic speciation and individuality. It is the increase in noncoding region and HERV sequences of the genome that led to the evolution of the primate and the human brain and its attendant property of conscious and quantal perception. It is the noncoding region of the genome with its archaeal, RNA viroidal complementary DNA and HERV sequences that makes for the human qualities of the hominid brain. Changes in the length of noncoding region can lead onto disorders of consciousness like schizophrenia. A schizophrenia specific human endogenous retroviruses and change in the length and grammar of the noncoding region has been described in schizophrenia.[33, 34]

An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described. Metal actinides in beach sands have been postulated to play a role in abiogenesis. Cholesterol is the primal prebiotic molecule synthesised on actinide surfaces with all other biomolecules arising from it. A self replicating cholesterol lipid organism could be the initial life form. A cholesterol based abiogenesis is a more likely evolutionary option and the actinidic archaea and viroids would have evolved from it. The origin of viruses, prokaryotes, eukaryotes, primates and humans from the initial isoprenoid organism derived actinidic archaea is discussed.

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Chapter 7

Endosymbiotic Pathogenic Archaea and Archaeal Derived RNA Viroids Induced Evolutionary Species Change in Humans - Interconversion of Homo Sapiens and Homo Neanderthalis - Method for Archaeal Symbiosis Modulated Human Evolution for Therapeutic Purpose

Introduction

The endosymbiotic archaea regulates human functions and species type and depends upon the colonic archaea whose density is determined by the fibre intake. The colonic archaeal population density depends upon dietary fibre intake. Populations with low fibre intake have lesser density of colonic archaeal microflora and endosymbiotic archaea. Endosymbiotic archaea contributes to neanderthalisation of the species. Populations consuming a high saturated fat and protein diet with low fibre intake tend to get increased endosymbiotic archaeal growth and are neanderthalised. Populations with high fibre intake up to 80 g/day tend to have reduced archaeal density in the colon and reduced archaeal endosymbiosis contributing to homo sapienisation of the population. Thus fibre intake regulates the endosymbiotic archaeal density and type of human species.

Archaeal symbiosis leads to neanderthalisation of the homo sapien species. This can be described as symbiosis mediated evolution. The homo neoneanderthalis has an increase predilection to metabolic syndrome X, strokes, CAD, hyperlipidemia, diabetes mellitus, autoimmune, neuropsychiatric, neurodegenerative, cancer and are retroviral resistant. The homo neanderthalis has different personality and social characteristics with increased creative, gender equal, matriarchal, asexual and alternate sexual, spiritual, intuitive, surrealistic and community centred characteristics. The homo sapien species are resistant to metabolic syndrome X, strokes, CAD, hyperlipidemia, diabetes mellitus, autoimmune, neuropsychiatric, neurodegenerative, cancer and are retroviral susceptible. The homo sapien species is less creative, patriarchal, gender unequal, heterosexual, logical and individualistic. Neanderthal metabolonomics is primarily mediated by archaeal metabolonomics and archaeal symbiosis. They have got cholesterol catabolism, the shikimic acid pathway, more of anaerobic glycolysis, increase connective tissue synthesis,

fructolysis, nucleic acid synthesis and mitochondrial dysfunction. Homo sapien metabolonomics is primarily aerobic and mitochondrial. The species change is a gut microflora and endosymbiotic flora mediated change which can be termed as induced evolution. Induction of species change between homo sapiens and homo neanderthalis was induced by feeding: (1) a natural organic probiotic from human colonic flora homo sapiens flora versus neanderthalis flora depending upon phenotypic characteristics. The homo sapien flora can induce conversion of neanderthalis to sapien species and the neanderthalis flora can induce conversion of sapiens to neanderthalis species, (2) a new paleo high fibre, high medium chain triglyceride, high legume protein ketogenic diet versus a high fat high protein diet. The high fibre high MCT high legume protein ketogenic diet converts the neanderthalis to sapien species and a low fibre high protein high fat diet converts the sapien species to neanderthalis species, (3) a natural organic probiotic from dung of the Indian cow, Bos primigenius which converts the neanderthalis to homo sapien phenotype and, (4) a natural antioxidant antibiotics derived from crude extracts Curcuma longa, Moringa pterygosperma, Emblica officinalis, Zingiber officinale, Allium sativum and Withania somnifera for modulation of endosymbiotic archaeal growth and endogenous digoxin synthesis resulting in phenotypic metabolonomic and genotypic change in human species from homo sapiens to homo neanderthalis. The colonic and endosymbiotic archaea and other microbes like clostridial clusters determine the species, race, caste, community and personal identity of the individual. The identity of the individual-personal, community, caste, race, nationality and species is determined by the colonic and endosymbiotic archaeal and clostridial clusters. Predominant archaeal symbiosis produces homo neanderthalis and less prominent archaeal symbiosis and dominant clostridial clusters in the gut produces the homo sapien species. Each individual, race, nationality, caste, creed and community has the endosymbiotic and colonic

microbiota signature. This colonic and endosymbiotic microbiota signature is transferable by the change of endosymbiotic and colonic microbiota from one group to another. Thus the evolution and identity based on individuality, race, nationality, caste and creed can be induced.

The research work carried out by us over a period of years showed that patients of these disorders mentioned show:

1. Decrease in the activity of a cell membrane based enzyme known as sodium potassium ATPase. An inhibition of sodium potassium ATPase produces increase in intracellular calcium and decrease in intracellular magnesium.
2. Membrane sodium potassium ATPase inhibition is produced by endogenous digoxin which is synthesized from cholesterol by actinidic archaea which acts as endosymbionts in cell. The archaea synthesizes digoxin from cholesterol.
3. Actinidic archaeal growth has been detected in metabolic syndrome X, coronary artery diseases, strokes, diabetes mellitus, hyperlipidemia, autoimmune, neuropsychiatric, neurodegenerative, cancer and infections
4. The paleo probiotic from human colonic flora are anti-archaeal agents. The paleo probiotic block the archaeal mevolanate pathway. This decreases digoxin synthesis from cholesterol and treats these chronic disorders.

Detection of Endogenous Actinidic Archaea

Endogenous actinidic archaea have been detected in metabolic syndrome X, diabetes mellitus, CAD, stroke, autism, autoimmune, neuropsychiatric, neurodegenerative, cancer and infections. The archaea are detected by spectrophotometry for cytochrome F420, the methanogenic cytochrome in the blood. The endogenous actinidic archaea synthesizes cholesterol by the

mevalonate pathway. The cholesterol is catabolized to digoxin. Digoxin inhibits membrane sodium-potassium-ATPase and increases intracellular calcium and depletes magnesium stores in the cell. This leads to metabolic syndrome X, diabetes mellitus, CAD, stroke, autism, autoimmune, neuropsychiatric, neurodegenerative, cancer and infections. The synthesis of digoxin can be demonstrated in patients by adding cholesterol substrate and cerium to patient's serum and checking for the rise in cytochrome F420 activity and digoxin levels. Digoxin levels are assayed by Elisa and cytochrome F420 by spectrophotometry. The test is available in the Metabolic Disorders Centre. The patient in whom endogenous archaea and digoxin synthesis is demonstrated is given nutritional dietary supplements to modulate the effects of archaea and digoxin. This helps to ameliorate the chronic diseases like metabolic syndrome X, diabetes mellitus, CAD, stroke, autism, autoimmune, neuropsychiatric, neurodegenerative, cancer and infections. Cytochrome F420 activity in the blood determines the homo neanderthalis species and lack of cytochrome F420 activity in the blood determines the homo sapien species. The homo neoneanderthalis has an increase predilection to metabolic syndrome X, strokes, CAD, hyperlipidemia, diabetes mellitus, autoimmune, neuropsychiatric, neurodegenerative, cancer and are retroviral resistant. The homo neanderthalis has different personality and social characteristics with increased creative, gender equal, matriarchal, asexual and alternate sexual, spiritual, intuitive, surrealistic and community centred characteristics. The homo sapien species are resistant to metabolic syndrome X, strokes, CAD, hyperlipidemia, diabetes mellitus, autoimmune, neuropsychiatric, neurodegenerative, cancer and are retroviral susceptible. The homo sapien species is less creative, patriarchal, gender unequal, heterosexual, logical and individualistic. Neanderthal metabolonomics is primarily mediated by archaeal metabolonomics and archaeal symbiosis. They have got cholesterol catabolism, the shikimic acid pathway, more of anaerobic glycolysis, increase connective

tissue synthesis, fructolysis, nucleic acid synthesis and mitochondrial dysfunction. Homo sapien metabolonomics is primarily aerobic and mitochondrial. The species change is a gut microflora and endosymbiotic flora mediated change which can be termed as induced evolution

Main Objectives of the Study

The gut microflora regulates body functions. The microflora modulates the immune system, the neuronal system and endocrine system. Alteration in the gut microflora as well as endosymbiotic bacteria has been related to human disease and evolution of human species. Increase in archaeal growth has been related to psychiatric disorders, tumours, autoimmune disease, metabolic syndrome and degenerations. The archaea forms a major chunk of the gut microflora. The archaea can leach into the tissue systems forming endosymbionts which can function like cellular organelle and can catabolise cholesterol. The symbiotic archaea can produce a Warburg phenotype and stem cell transformation. This can lead onto human diseases-psychiatric disorders, tumours, autoimmune disease, metabolic syndrome and degenerations. The overgrowth of symbiotic archaea can lead onto change in human species type and create a species with Neanderthal metabolonomics. This disease process leading onto psychiatric disorders, tumours, autoimmune disease, metabolic syndrome and degenerations can be reversed by altering the gut microflora and populating it with non-archaeal phenotypes. This can be done by oral administration of fecal microflora from healthy population.

Symbiosis by microorganisms especially archaea drives the evolution of the species. In such a case symbiosis can be modulated by transfer of microflora symbionts and evolution induced. Endosymbiosis by archaea as well as archaeal symbionts in the gut can modulate the genotype, the phenotype, the social class

and the racial group of the individual. The symbiotic archaea can have horizontal and vertical transmission. Endosymbiotic archaeal growth leads to neanderthalisation of the species. The inhibition of the endosymbiotic archaeal growth on the other hand leads to evolution of the homo sapiens. Symbiosis mediated evolution depends on the gut flora and the diet. The combination of the human genome and the symbiotic microbial genome is called the hologenome drives human evolution as well as animal evolution. Endosymbiotic archaeal growth and neanderthalisation can lead to autoimmune disease, metabolic syndrome X, neurodegeneration, cancer, autism and schizophrenia. The Neanderthal gut flora and endosymbiotic archaea was determined by the non vegetarian ketogenic high fat high protein diet consumed by them in the Eurasian steppes. The homo sapiens including the classical Aryan tribes and African ate a high fibre diet and had lower archaeal growth both endosymbiotic and gut. The dietary fibre intake determines the microbial diversity of the gut. The high fibre intake is associated with increased generation of short chain fatty acids-butyric acid by the gut flora. Butyrate is a HDAC inhibitor and leads to increased generation and incorporation of endogenous retroviral sequences which function as jumping genes. The high dietary fibre intake related increased genomic HERV sequences leads to a dynamic genome, increased synaptic connectivity and a dominant frontal cortex as seen in homo sapien species. The neanderthalic species consume a ketogenic non vegetarian high fat high protein low fibre diet. This leads to decreased generation of endogenous HERV sequences and reduced genomic flexibility in neanderthalic species. This produces smaller cerebral cortex and a dominant cerebellar cortex in the neanderthalic brain. The homo neanderthalic species by the low dietary fibre intake starve their microbial self. This leads to increased endosymbiotic and gut archaeal growth. The mucous membrane lining the gut becomes thinned out as the gut bacteria eats up the mucous lining of the gut.

The reduced generation of gut butyrate consequent to increased archaeal growth also damages the gut blood and blood brain barrier. This results in leakage of endotoxins and archaea from the gut to the blood breaching the barrier and produces a chronic immunostimulatory inflammatory state which forms the basis of autoimmune disease, metabolic syndrome, neurodegeneration, oncogenic and psychiatric disorders. The Neanderthal species eat a low fibre diet and have a deficiency of microbiota accessed carbohydrate generating short chain fatty acid. There is a deficiency of butyrate generated in the gut from the dietary fibre which can produce suppression of the chronic inflammatory process. The Neanderthals have got the fermentation by-product deficiency syndrome. The induction of neanderthalic species depends on the low fibre intake induced high archaeal density endosymbiotic and the gut microflora. The homo sapiens species consume a high fibre diet generating large amounts of short chain fatty acid butyrate which inhibits endosymbiotic and gut archaeal growth. The microbial self of the homo sapien species is more diverse than that of the neanderthalic species and the archaeal population density is less. This results in a protection against chronic inflammation and the induction of diseases like autoimmune disease, metabolic syndrome, neurodegeneration, oncogenic and psychiatric disorders. The homo sapien species have a higher intake of dietary fibre contributing to around 40 g/day and a diverse microbial gut flora with less of archaeal population density. The butyrate generated from dietary fibre produces an immunosuppressive state. Thus the symbiotic microflora with less of archaeal density induces a homo sapien species. This can be demonstrated by experimental induction of evolution. A high fibre high MCT diet as well as antibiotics derived from higher plants and fecal microbiota transfer from sapien species can inhibit the Neanderthal metabolonomics and phenotype and induce the evolution of homo sapiens. A low fibre high fat high protein diet as well as fecal microbiota transfer from the Neanderthal species

can produce Neanderthal metabolonomics and phenotype inducing the evolution of homo neanderthalis. Transfer of colonic microflora predominantly archaea and modulation of endosymbiotic archaea by a paleo diet and antibiotics from higher plants can lead to interconversion of human species between homo neanderthalis and homo sapiens. The hologenome especially the microbial flora endosymbiotic/gut drives human and animal evolution and can be experimentally induced. Symbiotic microflora drives evolution. Every animal, every human species, different communities, different races and different caste have their signature endosymbiotic and gut microflora which can be transmitted vertically and horizontally. Thus symbiosis drives human and animal evolution.

Methods for Species Change - Colonic Flora Probiotic Administration from Homo Sapiens and Homo Neanderthalis Identified by Blood Cytochrome F420 Activity

Research work carried out by us over a period of years has shown patients have this disorders or condition show a significant improvement on the natural organic paleo probiotic when endogenous archaeal growth and digoxin synthesis is demonstrated in the patients. Populations are screened for endosymbiotic archaeal activity in the sera by analysis of cytochrome F420 activity. The population that is negative for cytochrome F420 activity is chosen for the collection of the specimen. The blood cytochrome F420 negative population was taken as homo sapien phenotype. The population was fed on a paleo diet of high dietary fibre, high medium chain triglyceride and pulse/legume protein. The normal fecal collection was done from a healthy normal genetically related individual chosen by the patient and the administration of the organic natural probiotic isolated from the genetically related individual was volitional and a patient decision. The permission of the

Ethics committee of the Institute - Metabolic Disorders Research Centre, Trivandrum was obtained. The fresh fecal matter from healthy humans was collected. Around 100 g of the organic matter is used in the preparation of the product. 100 g of the organic matter is diluted with normal saline and centrifuged at 2500 rpm. The rough matter forms a deposit and the supernatant is collected. The supernatant is preserved by adding 25 g of trehalose which can preserve the probiotic bacteria. This supernatant with added trehalose is freeze-dried and packed in double gelatin capsules. This capsule can be administered orally. The population with homo sapien characteristics was given fecal colonic flora preparation from neanderthalic phenotypes in the manner described above. The neanderthalic phenotypes were cytochrome F420 positive in their blood. Thus interconversion of species was possible by administration of probiotic from colonic flora of homo sapiens and homo neanderthalis identified by cytochrome F420 activity in blood.

Methods for Species Change-High Fibre Diet Versus Low Fibre Diet

High archaeal growth induces neanderthalisation of human species. Neanderthal metabolonomics leads to chronic diseases like metabolic syndrome X, diabetes mellitus, CAD, stroke, autism, autoimmune, neuropsychiatric, neurodegenerative, cancer and infections. The patient in whom endogenous archaea and digoxin synthesis is demonstrated is given high fibre, legume protein and high medium chain triglyceride ketogenic diet along with natural antibiotics Curcuma longa, Moringa pterygosperma and Emblica officinalis ketogenic diet to modulate the effects of archaea and digoxin. This helps to convert the Neanderthal phenotype to homo sapien phenotype. Research work carried out by us over a period of years has shown neanderthalised species with civilisational disease as mentioned above show a significant improvement on

the following combination when endogenous archaeal growth and digoxin synthesis is inhibited by a high fibre ketogenic diet derived from: (1) Curcuma longa, (2) Emblica officinalis, (3) Powdered Moringa pterygosperma, (4) Whole coconut powder, (5) Powdered black gram and, (6) Powdered dried ash gourd. The individual materials were frozen dried and powdered to get 100-200 micron size. Then they were mixed at a concentration of: (1) 10 g of Curcuma longa - A, (2) 10 g of Emblica officinalis - B, (3) 100 g of whole coconut powder - C, (4) 100 g of dried Moringa pterysperma leaves - D, (5) 100 g of powdered dried black gram - E and, (6) 100 g of powdered dried ash gourd - F. Components A, B, C, D, E and F were mixed to form a packet of 420 g. They were then mixed thoroughly and made into 420 g packet. They were assessed before treatment was started by clinical examination and lab investigations. The duration of the treatment ranged from 6 months to 2 years. We found that in the case tried high fibre, legume protein and high medium chain triglyceride ketogenic diet along with natural anti-biotics Curcuma longa, Moringa pterygosperma and Emblica officinalis showed significant curative effects. None of the substance used or information used in combination as described above for the purpose described to use have been used before. The consumption of a high fibre diet resulted in conversion of the homo neanderthalis species to homo sapien species. The high fibre diet results in reduction of gut archaeal growth and decreased endosymbiotic archaeal growth. The gut butyrate production is increased and the gut blood barrier and blood brain barrier is strengthened. The homo sapien species when fed a low fibre high fat high protein non-vegetarian diet has increased density of gut archaeal microflora and endosymbiotic archaeal growth. The gut butyrate generation is reduced and the gut blood barrier and blood brain barrier is breached. This leads to increase in endosymbiotic archaea and the homo sapien species gets converted to homo neanderthalis species.

Method of Interconversion of Human Species by Administering Colonic Microflora from Cow Dung

Archaeal symbiosis results in neanderthalisation of human species and civilisational diseases like metabolic syndrome X with diabetes mellitus and vascular disease, Autoimmune, Neuropsychiatric, Neurodegenerative, Cancer, Infections. This invention relates to a formulation which will act as a natural organic paleo probiotic from dung of the Indian cow, Bos primigenius for various diseases which will inhibit archaeal growth and convert homo neanderthalis to homo sapiens. This disease process leading onto psychiatric disorders, tumours, autoimmune disease, metabolic syndrome and degenerations can be reversed by altering the gut microflora and populating it with non-archaeal phenotypes. This can be done by oral or rectal administration of fecal microflora of the Indian cow, Bos primigenius. The cow chosen for the purpose was the Indian cow, Bos primigenius. The Indian cow fed an organic diet of grass and hay was chosen for the purpose. The administration of the organic natural probiotic isolated from the genetically related individual was volitional and a patient decision. The permission of the Ethics committee of the Institute - Metabolic Disorders Research Centre, Trivandrum was obtained. The fresh fecal matter from healthy the Indian cow, Bos primigenius are collected. Around 100 g of the organic matter is used in the preparation of the product. 100 g of the organic matter is diluted with normal saline and centrifuged at 2500 rpm. The rough matter forms a deposit and the supernatant is collected. The supernatant is preserved by adding 25 g of trehalose which can preserve the probiotic bacteria. This supernatant with added trehalose is freeze-dried and packed in double gelatin capsules. This capsule can be administered orally or as a rectal enema. Thus feeding of the colonic microflora from cow dung resulted in conversion of the Neanderthal metabolonomics to homo sapien metabolonomics.

Method of Interconversion of Species - Antioxidant Antibiotics

Archaeal symbiosis leads to neanderthalisation of the species with increased incidence of metabolic syndrome X, diabetes mellitus, CAD, stroke, autism, autoimmune, neuropsychiatric, neurodegenerative, cancer and infections. The patient in whom endogenous archaea and digoxin synthesis is demonstrated is given natural antioxidant antibiotics derived from crude extracts Curcuma longa, Moringa pterygosperma, Emblica officinalis, Zingiber officinale, Allium sativum and Withania somnifera to modulate the effects of archaea and digoxin. This converts the Neanderthal phenotype to homo sapien phenotype. Research work carried out by us over a period of years has shown patients have this disorders or condition show a significant improvement on the following combination when endogenous archaeal growth and digoxin synthesis is demonstrated in the patients: (1) Curcuma longa, (2) Emblica officinalis, (3) Powdered Moringa pterygosperma, (4) Powdered Zingiber officinale, (5) Powdered Allium sativum, (6) Powdered Withania somnifera root and leaves. The individual materials were frozen dried and powdered to get 100-200 micron size. Then they were mixed at a concentration of: (1) 10 g of Curcuma longa - A, (2) 10 g of Emblica officinalis - B, (3) 10 g of powdered Moringa pterygosperma - C, (4) 10 g of powdered Zingiber officinale - D, (5) 10 g of powdered Allium sativum - E and, (6) 10 g of powdered Withania somnifera root and leaves - F. Components A, B, C, D, E and F were mixed to form a packet of 60 g. They were then mixed thoroughly and made into 60 g packet. They were assessed before treatment was started by clinical examination and lab investigations. The duration of the treatment ranged from 6 months to 2 years. We found that in the case tried natural antioxidant antibiotics derived from crude extracts Curcuma longa, Moringa pterygosperma, Emblica officinalis, Zingiber officinale, Allium sativum and Withania somnifera showed significant curative effects. None of the substance used or information

used in combination as described above for the purpose described to use have been used before.

Details of the Trial

Archaeal symbiosis leads to neanderthalisation of the homo sapien species. This can be described as symbiosis mediated evolution. The homo neoneanderthalis has an increase predilection to metabolic syndrome X, strokes, CAD, hyperlipidemia, diabetes mellitus, autoimmune, neuropsychiatric, neurodegenerative, cancer and are retroviral resistant. The homo neanderthalis has different personality and social characteristics with increased creative, gender equal, matriarchal, asexual and alternate sexual, spiritual, intuitive, surrealistic and community centred characteristics. Neanderthal metabolonomics is primarily mediated by archaeal metabolonomics and archaeal symbiosis. They have got cholesterol catabolism, the shikimic acid pathway, more of anaerobic glycolysis, increase connective tissue synthesis, fructolysis, nucleic acid synthesis and mitochondrial dysfunction. Self administration of the natural organic paleo probiotic from human colonic flora and cow dung, antioxidant antibiotic and high fibre high MCT diet to neanderthalised phenotype with pathological phenotypes of the following disorders. (1) Primary generalized epilepsy, (2) Schizophrenia, (3) Parkinson's disease, (4) Multiple sclerosis, (5) Refractory CNS glioblastomas, (6) Neuronal aging and dementia of the Alzheimer's type, (7) Down's syndrome, (8) Acquired immunodeficiency syndrome, (9) Autism, (10) CAD, (11) Stroke, (12) Diabetes mellitus, and (13) Aging. The patients were assessed before treatment was started clinically and by all required laboratory investigations. The duration of treatment ranged from 6 months to 2 years. Their condition was assessed during treatment and after treatment clinically and using all necessary laboratory investigations. This produced a change in the homo neanderthalis phenotype to homo sapien phenotype.

The homo sapien species are resistant to metabolic syndrome X, strokes, CAD, hyperlipidemia, diabetes mellitus, autoimmune, neuropsychiatric, neurodegenerative, cancer and are retroviral susceptible. The homo sapien species is less creative, patriarchal, gender unequal, heterosexual, logical and individualistic. Homo sapien metabolonomics is primarily aerobic and mitochondrial. The species change is a gut microflora and endosymbiotic flora mediated change which can be termed as induced evolution. The feeding of the homo sapien phenotype with a low fibre high fat high protein non-vegetarian diet resulted in increased in archaeal density in the gut microflora and endosymbiotic archaeal growth in the blood as measured by cytochrome F420 activity and neanderthalisation of the homo sapien species. This makes the homo sapien species neanderthalised with a different phenotype, genotype, psychological type and retroviral resistant.

Patient Population Included in the Large Scale Trial of Neanderthalised Phenotype

These are typical examples of a large number of patients tried in each case. The number of patients included in the trial is as follows. The neanderthalised phenotypes were fed a high fibre, high MCT vegetarian diet, colonic microflora probiotic from blood cytochrome F420 negative homo sapien population, colonic microflora from the Indian cow dung Bos primigenus and antioxidant antibiotic for 6 months showed conversion to homo sapien phenotypes with low blood cytochrome F420 activity and statistically significant disease remission. The psychological characters changed from neanderthalic increased creative, gender equal, matriarchal, asexual and alternate sexual, spiritual, intuitive, surrealistic and community centred characteristics to homo sapien less creative, patriarchal, gender unequal, heterosexual, logical and individualistic. The metabolic phenotype changed from neanderthalic cholesterol catabolism, the

shikimic acid pathway, more of anaerobic glycolysis, increase connective tissue synthesis, fructolysis, nucleic acid synthesis and mitochondrial dysfunction phenotype to homo sapien mitochondrial phenotype.

1. Primary generalized epilepsy - 25 patients.
2. Schizophrenia - 25 patients.
3. Parkinson's disease - 25 patients.
4. Multiple sclerosis - 25 patients.
5. Refractory CNS glioblastoma - 15 patients
6. Diabetes mellitus - 50 patients
7. Neuronal aging and dementia of the Alzheimer's type - 25 patients
8. Down's syndrome - 15 patients
9. Acquired immunodeficiency syndrome - 15 patients
10. Autism - 50 patients
11. CAD - 50 patients
12. Stroke - 50 patients
13. Lupus syndrome - 25 patients

Patient population included in the large-scale trial of homo sapien phenotype identified by lower or absent cytochrome F420 activity in blood. They were fed a low fibre, high fat, high protein, non-vegetarian diet for 6 months. This resulted in increase in endosymbiotic and colonic archaeal density and neanderthalisation of the homo sapien phenotype. The homo sapien phenotype given colonic microflora capsules from normal Neanderthal phenotypes with high cytochrome F420 activity also resulted in neanderthalisation of homo sapien phenotype. The psychological characteristics changed from homo sapien

less creative, patriarchal, gender unequal, heterosexual, logical and individualistic to neanderthalic increased creative, gender equal, matriarchal, asexual and alternate sexual, spiritual, intuitive, surrealistic and community centred characteristics. The metabolic phenotype changed from homo sapien mitochondrial phenotype to neanderthalic cholesterol catabolism, the shikimic acid pathway, more of anaerobic glycolysis, increase connective tissue synthesis, fructolysis, nucleic acid synthesis and mitochondrial dysfunction phenotype.

Summary

A method to induce evolutionary changes in the human species by modulating archaeal symbiosis and interconverting homo sapien to homo neanderthalis and vice versa is described. This is done by a high fibre versus a low fibre diet, administration of antioxidant antibiotic and colonic microflora from human and cow dung. This is a methodology to modulate species interconversion from homo sapien to homo neanderthalis with its attendant changes in psychological, phenotypic and metabolonomic characteristics of the population. This can be called as a therapeutic archaeal symbiotic modulated human evolution.

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