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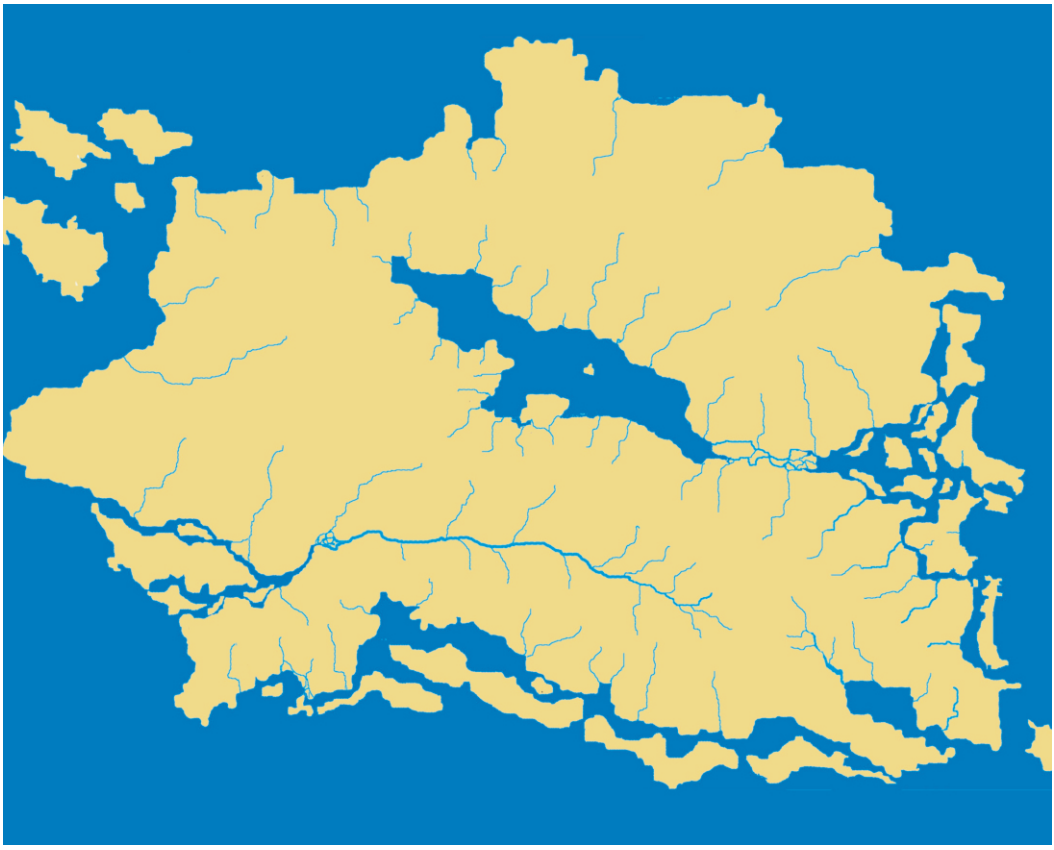
Global Warming, Archaea and Viroid Induced Symbiotic Human Evolution – Lemurian Syndrome - Endomyocardial Fibrosis, Chronic Calcific Pancreatitis, Multinodular Goitre and Mucoid Angiopathy - The Glycosaminoglycoid Organelle



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The Endosymbiotic Archaea, Fructose Disease, Lemurian Syndrome and Global Warming

Global warming induces endosymbiotic archaeal and RNA viroidal growth. The porphyrins form a template for the formation of RNA viroids, DNA viroids, prions, isoprenoids and polysaccharides. They can symbiose together to form primitive archaea. The archaea can further induce HIF alpha, aldose reductose and fructolysis resulting in further porphyrinogenesis and archaeal self replication. The primitive archaeal DNA is integrated along with RNA viroids which are converted to their corresponding DNA by the action of redox stress induced HERV reverse transcriptase into the human genome by the redox stress induced HERV integrase. The archaeal DNA sequences that are integrated into the human genome forms endogenous archaeal human genomic sequences akin to HERV sequences and can function as jumping genes regulating genomic DNA flexibility. The integrated endogenous genomic archaeal sequences can get expressed in the presence of redox stress forming endosymbiotic archaeal particles which can function as a new organelle called the archaeaons. The archaeaon can express the fructolytic pathway constituting an organelle called the fructosome, cholesterol catabolic pathway and digoxin synthetic forming an organelle called the steroidelle, the shikimic acid pathway forming an organelle called the neurotransminoid, antioxidant vitamin E and vitamin C synthetic organelle called the vitaminocyte as well as the glycosaminoglycan synthetic organelle called glycosaminoglycoid. The archaea can secrete capsulated RNA viroidal particles which can function as blocking RNAs modulating cell metabolism and such archaeaon organelle are called viroidelle. The archaea suppresses pyruvate dehydrogenase and promotes fructolysis resulting in accumulation of pyruvate which enters the GABA shunt pathway producing succinyl CoA and glycine, the substrates for porphyrin synthesis. Porphyrin forms a template for the formation of RNA viroids, DNA viroids, prions and isoprenoids which can symbiose together to form an archaea. Thus endosymbiotic archaea have an abiogenic replication. The archaeaon concerned

with GABA shunt pathway and porphyrinogenesis are called porphyrinoids. The archaeaon colony forms a network with different areas showing differential specialization of function - fructosoids, steroidelle, vitaminocyte, viroidelle, neurotransminoid, porphyrinoids and glycosaminoglycoids. This forms a living organized structure within human cells and tissues regulating their function and reducing the human body to zombie working under the directions of the organized archaeal colony. The organized archaeal colony has abiogenetic replication and is eternal.

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

global warming related Lemurian syndrome of EMF, CCP, MNG and mucoid angiopathy.

The endosymbiotic actinidic archaea forms the basis of life and can be considered as the third element in the cell. It regulates the cell, the neuro-immune-endocrine system and the conscious / unconscious brain. The endosymbiotic actinidic archaea can be called as the elixir of life. A definite population of endosymbiotic actinidic archaea is required for the existence and survival of life. A higher density of endosymbiotic actinidic archaeal population can lead to human disease. Thus actinidic archaea are important for survival of human life and can be considered as crucial to it. Symbiosis by actinidic archaea is the basis of evolution of humans and primates. The increase in endosymbiotic archaeal growth can lead to the induction of homo neanderthalis. This endosymbiotic archaea induced neanderthalisation of the species leads to human disease like metabolic syndrome X, neurodegenerations, schizophrenia and autism, autoimmune disease and cancer. The reduction in endosymbiotic archaeal growth by a high fibre, high medium chain triglyceride and legume protein ketogenic diet, antibiotics from higher plants like Curcuma longa, Emblica officianalis, Allium sativum, Withania somnifera, Moringa pterygosperma and Zingeber officianalis and transplantation of colonic microflora from normal homo sapien population can lead to deneanderthalisation of species and treatment of the above mentioned diseased states. The colonic microflora of neanderthalised diseased states like metabolic syndrome X, neurodegenerations, schizophrenia and autism, autoimmune disease and cancer when transferred to the normal homo sapien species leads to generation and induction of homo neanderthalis. Thus primate and human evolution is symbiotic event which can be induced the modulating symbiotic archaeal growth. Human populations can be divided into matrilineal Neanderthal population in South Indian Dravidians, Celts, Basques, Jews and

Berbers and the Cro-Magnon population seen in Africa and Europe. The symbiotic archaeal colonization decides which species - Neanderthal or Cro-Magnon to which the society belongs to. It is tempting to postulate symbiotic microflora and archaea determining the family behavior and traits as well as societal and caste behavior and traits. The cell has been postulated by Margulis to be a symbiotic association of bacteria and viruses. Similarly, the family, the caste, the community, nationalities and the species itself is determined by archaeal and other bacterial symbiosis.

Symbiosis by microorganisms especially archaea drives the evolution of the species. In such a case symbiosis can be induced 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 neanderthalised species is matrilineal society and includes the Dravidians, the Celts, the Basques and the Berbers. The inhibition of the endosymbiotic archaeal growth leads to evolution of the homo sapiens. This includes the Africans, Aryan invaders of North India and the Aryan derived European population. Symbiosis mediated evolution depends on the gut flora and the diet. This has been demonstrated in the drosophila pseudoobscura. The drosophila mates only with other individuals eating the same diet. When the drosophila gut microflora is altered by feeding antibiotics they mate with other individuals eating different diets. The diet consumed by the drosophila regulates its gut microflora and mating habits. The combination of the human genome and the symbiotic microbial genome is called the hologenome. The hologenome especially its symbiotic microbial component drives human evolution as well as animal evolution. The evolutionary distance between species of wasp depends on the gut microflora. The human gut

microflora regulates the endocrine, genetic and neuronal systems. Humans and primate evolution depends on endosymbiotic archaea and gut microflora. The endosymbiotic archaeal growth determines the racial differences between the matrilineal Harappan / Dravidian societies and the patriarchal Aryan society. The matrilineal Harappan / Dravidian society was neanderthalic and had increased endosymbiotic archaeal growth. 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. The high dietary fibre intake related increased HERV sequences leads to 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. This results in leakage of endotoxin 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.

This can be interpreted on the basis of Villarreal hypothesis of group identity and cooperativity of RNA collectives. Archaeal symbiosis in the gut and in the tissue spaces determines speciation of human beings as homo sapiens and homo neanderthalis. The endosymbiotic archaea can secrete RNA viroids and viruses and there is a viroid-archaeal host relationship between the two. A dynamic state of virus lysis and persistence can occur in archaea suggesting that viral addiction can occur in archaea. The RNA viroids in the archaea coordinate their behavior by information exchange, modulation and innovation generating new sequence based content. This occurs due to a phenomenon of symbiosis in contrast to the concept of survival of the fittest. The generation of new RNA viroidal sequences is a result of practical competence of living agents to generate new sequences by symbiosis and sharing. This represents highly productive RNA viroidal quasi-species consortia for the evolution, conservation and plasticity of genomic environments. The behavioural motives of the RNA are single stem loop structures. They have self folding and group building capabilities depending upon functional needs. The evolution process depends upon what Villareal calls RNA stem loop consortia. The whole entity can function only if participatory groups of RNA viroids can get their function coordinated. There is competent denovo generation of new sequences by cooperative action and not by competition. These RNA viroidal group consortia can contribute to the host identity, group identity and group immunity. The term used for this is RNA viroidal sociological behavior. The RNA viroids can build

groups that invade the archaea and compete as a group for limited resources such host genomes. A key behavioural motif is able to integrate a persistent life style into the archaeal colony with the addiction module forming competing viroidal groups that are counter balancing each other together with the archaeal/host immune system. This leads to creation of an identity for the archaeal colony and the homo neanderthalis host. Viroids can kill their host and also colonize their host without disease and protect the host from similar viruses and viroids. Together with lysis and protection we see a viroid colonized host that is both symbiotic and innovative acquiring new competent codes. Thus the viroid-host relationship is a pervasive, ancient force in the origin and evolution of life. Cumulative evolution at the level of RNA viroids is like a ratchet effect used for transmission of cultural memes. This learning accumulates so that every new generation must not repeat all innovative thoughts and techniques. Quasi-species of RNA viroids are cooperative and exclusive of other quasi-species. They have group recognition differentiating self-groups and non-self-groups allowing for quasi-species to promote the emergence of group identity. With group identity via counter related addiction modules two opposing components must be present and work coherently and define the group as a whole. Biological identity is constituted by dynamic interaction of cooperative groups. Virus addiction module is an essential strategy for existence of life in the virosphere. Viruses are transmissible and can persist in specific host population leading to a form of group immunity / identity since identical but uncolonized host population remains susceptible to a killing action of lytic viruses. In this way we see that viruses are necessary providing opposing functions for addiction (persistence/protection and lytic/killing). Viroids can function as consortia, an essential interacting group and provide a mechanism from which consortial function could emerge in the origin of protobiotic life. Genetic parasites can act as a group (qs-c). But for this group to be coherent

they must attain group identity and this is typically via an addiction strategy. Antiviral and proviral system in the archaea will themselves emerge in the host from virus derived information. The archaeal viruses themselves provide the critical function required for antiviral defence. The opposing functions are the basis of addiction modules. Thus the emergence of group identity becomes an essential and early event in the emergence of life. This is coherent to the basically group behavior of RNA viroids in archaea. This group selection and group identity are needed to create information coherence and network formation and to establish a system of communication - code competent interactions. This identity serves as information also for the ones that do not share this identity. This is the beginning of self/non-self differentiating capability. In this way viroids promote the emergence of group identity in archaeal colonies and host humans. The archaeal colony identity depends upon the colonizing set of RNA viroids producing a coherent network that is inclusive opposing functions and favours the persistence of parasite derived new information. On the basis of population-based functions of RNA DNA can be considered as a habitat for consortia RNA. Thus RNA viroids of the archaea are involved in complex multicellular identity. This is called as the Gangen hypothesis by Villarreal. The Gangen describes the emergence of commonly shared code use, group membership and collective living function of RNA viroids. Communication is a code depended interaction and transmission of infectious code defines the origin of the virosphere. This issue refers to the idea of collective of RNA viroids with inherent toxic and antitoxic features should be able to transmit or communicate these agents and their features to a nearby competing population. It strongly favours the survival of RNA viroidal population with compatible addiction modules that will inhibit agent toxicity and allow persistence of new agents. This is thus the survival of the persistently colonized set which is an inherently symbiotic and consortial process. It also

promotes increasing complexity and identity/immunity of the host collective via a new agent colonization, and stable addition. Thus the transmission of RNA agents attains both communication and recognition of group membership. In this way the emergence of the virosphere must had been an early event in the origin of life and group identity. Viruses and viroids are genetic parasites and the most abundant living entities on earth. The virosphere is a network of infectious genetic agents. Evolution, conservation and plasticity of genetic identities are the result of cooperative consortia of RNA viroids that are competent to communicate. Thus the archaeal viroidal consortia can symbiotically share and communicate producing new sequences and give an identity to the archaeal colony. The low fibre diet and extreme temperatures of the Eurasian steppes leads to archaeal multiplication and induction of the homo neanderthalis species. The archaeal colony's characteristics are determined by the cooperative consortia of RNA viroids in the archaea and the archaeal colony identity determines the homo neanderthalis identity. Thus the archaeal colonies with their quasi-species consortia of RNA viroids determine the homo neanderthalis identity. The new sequence generation by the RNA viroidal consortia's symbiotic sharing character contributes to the diversity in the behavior and creativity of the homo neanderthalis population. The archaeal RNA viruses and viroids and the archaeal colonies themselves protect the homo neanderthalis population from retroviral infections. Thus the homo neanderthalis population is retroviral resistant and the quasi-species consortia of archaea and archaeal viroids gives them a group identity as retroviral resistant. Thus the quasi-species consortia of archaea and RNA viroids give homo neanderthalis colonies their identity and idea of self. The homo neanderthalis is resistant to retroviral infection like the Australian aboriginals and the endogenous retroviral sequences in the Neanderthal genome are limited. This leads to lack of plasticity and dynamicity of the human genome and the cerebral

cortex in ill-developed with a dominant impulsive cerebellar cortex in the homo neanderthalis population. This produces the impulsive creative surrealistic spiritual neanderthalic brain. As the extreme of temperature goes off and the ice age ends the archaeal population density also comes down. This also can result from the consumption of a high fibre diet in the African continent. The high fibre diet digested by clostridial clusters in the colon promotes butyrate synthesis and butyrate will induce HDAC inhibition and expression of retroviral sequences in the primate genome. This leads to increase in endogenous retroviral sequences in the human genome, increasing genomic dynamicity and the evolution of complicated cerebral cortex dominant brain with its complex synaptic connectivity in the homo sapiens. This leads onto a logical, commonsensical, pragmatic and practical homo sapien brain. The homo sapiens due to lack of archaea and the RNA viroids are susceptible retroviral infection. Thus the archaeal colonies and RNA viroidal quasi-species consortia determine the evolution of the human species and the brain networks. Thus extremes of temperature, fibre intake, archaeal colony density, RNA viroidal quasi-species, group identity and retroviral resistance decides on the evolution of homo sapiens and homo neanderthalis as well as the brain networks. The present extremes of temperature and low fibre intake in civilized society can lead to increase in archaeal population densities and quasi-species RNA viroidal networks generating a new homo neanderthalis in a new neanderthalic anthropocene age as opposed to the present homo sapien anthropocene age.

The roots of Western civilisational disease can be related to the starvation of the colonic microflora. The colonic microflora depends upon complex carbohydrates derived from dietary fibre. The processed food of high protein, fat and sugars is digested and absorbed in the stomach and small intestine. A very little of it reaches the colon and widespread use of antibiotics in medicine has produced mass extinction of the colonic microflora. The colonic microflora

is extremely diverse and the diversity is lost. There are 100 trillion bacteria in the colon belonging to 1200 species. They regulate the immune system by inducing the T-regulatory cells. A high fibre diet contributes to colonic microbiota diversity. Interaction with farm animals like cows and dogs also contributes to the colonic microflora diversity. The typical Western diet of high fat, high protein and sugars decreases the colonic microbiota diversity and increase colonic/endosymbiotic archaea producing methanogenesis. The colonic archaea feed upon the mucous lining of the colon and produces leakage of archaea into the blood and tissue system producing endosymbiotic archaea. This results in a chronic inflammatory state. The high fibre diet of Africans, South Americans and Indians produces increased colonic microbiota diversity and increase in clostridial clusters generating SCFA in the gut. High fibre diet is protective against metabolic syndrome and diabetes mellitus. Metabolic syndrome is related to degeneration, cancer, neuropsychiatric illness and autoimmune disease. A high fibre diet of upto 40 g/day can be called as a gut diet. The colonic microflora especially the clostridial cluster digests the fibre generating short chain fatty acids which regulates immunity and metabolism. High fibre diet increases the colonic mucus secretion and the thickness of the mucus lining. A high fibre diet produces increase in clostridial clusters and mucous secretion. This produces a strong gut blood barrier and prevents metabolic endotoxemia which produces a chronic inflammatory response. High dietary fibre intake and the diversity of the colonic microflora with prominent SCFA producing clostridial clusters are interrelated. The clostridial clusters metabolise the complex carbohydrate in dietary fibre to short chain fatty acids butyrate, propionate and acetate. They increase the T-regulatory function. A high fibre diet increases the bacteroides and reduces the firmecutes of the colonic microflora. A high fibre diet is associated with a low body-mass index. A low fibre diet produces increase in colonic archaeal growth as well as

endosymbiotic tissue and blood archaea. This produces more of methanogenesis rather than short chain fatty acid synthesis contributing to immune activation. A low fibre diet is associated a high body-mass index and chronic systemic inflammation. Germ-free mice show cardiac, pulmonary and liver atrophy. Gut microflora is required for the generation of organ systems. The gut microflora is also required for generation of T-regulatory cells. High fibre intake produces more colonic microbiota diversity and increase in clostridial clusters and fermentation by products like butyrate which suppresses inflammation and increases T-regulatory cells. A low fibre diet produces increase in archaeal growth, methanogenesis, destruction of the mucus lining and leakage of the colonic archaea producing endosymbiotic tissue and blood archaea. This produces an immune hyperreactivity contributing to the modern plagues of civilisation - metabolic syndrome, schizophrenia, autism, cancer, autoimmunity and degenerations. The gut microbiota drives human evolution. The humans don't host the gut microbiota but the gut microbiota host us. The human system forms an elaborate culture laboratory for the propagation and survival of the microbiota. The human system is induced by the microbiota for their survival and growth. The human system exists for the microbiota and not the other way round. The same mechanism holds good in plant systems. Plant started the colonized earth as they started symbiosing with bacteria in the roots systems which can derive nutrients from the soil. Human beings form a mobile culture laboratory for the more effective propagation and survival of the microbiota. The microbiota induces the formation of specialized immune cells called innate lymphoid cells. The innate lymphoid cells will direct the lymphocytes not to attack the beneficial bacteria. Thus the endosymbiotic archaea and the gut archaea induce human, primate and animal evolution to generate structures for them to survive and propagate. The source of endosymbiotic archaea, the third element of life is the colonic archaea that leaks into the tissue spaces and blood

systems due to breach in the gut blood barrier. The increase in colonic archaea is due to the starvation of the gut microbiota consequent to a low fibre diet. This results in increase in colonic archaeal growth and destruction of clostridial clusters and bacteroides. The increase colonic archaeal growth in the presence of gut starvation due to low fibre diet eats up the mucus lining and produces breakages in the gut blood barrier. The colonic archaea enters the blood stream and produces endosymbiosis generating endosymbiotic archaea and various new organelle - fructosoids, steroidelle, vitaminocyte, viroidelle, neurotransminoid, porphyrinoids and glycosaminoglycoids.

The increase in endogenous EDLF, a potent inhibitor of membrane Na^+-K^+ ATPase, can decrease this enzyme activity. The results showed increased endogenous EDLF synthesis as evidenced by increased HMG CoA reductase activity, which functions as the rate limiting step of the isoprenoid pathway. Studies in our laboratory have demonstrated that EDLF is synthesized by the isoprenoid pathway. The endosymbiotic archaeal sequences in the human genome get expressed by redox stress and osmotic stress of global warming. This results in induction of HIF alpha which will upregulate fructolysis and glycolysis. In the setting of redox stress all glucose gets converted to fructose by the induction of enzymes aldose reductase and sorbitol dehydrogenase. Aldose reductase converts glucose to sorbitol and sorbitol dehydrogenase converts sorbitol to fructose. Since fructose is preferentially phosphorylated by ketohexokinases the cell is depleted of ATP and glucose phosphorylation comes to a halt. Fructose becomes the dominant sugar that is metabolized by fructolysis in expressed archaeal particles in the cell functioning as organelle called fructosoids. The fructose is phosphorylated to fructose 1-phosphate which is acted upon by aldolase B which converts it into glyceraldehyde 3-phosphate and dihydroxy acetone phosphate. Glyceraldehyde 3-phosphate is converted to D1,3-biphosphoglycerate which is then converted to

3-phosphoglycerate. The 3-phosphglycerate is converted to 2-phosphoglycerate. 2-phosphoglycerate is converted to phosphoenol pyruvate by the enzyme enolase. Phosphoenol pyruvate is converted to pyruvate by the enzyme pyruvic kinase. The archaeaon induces HIF alpha which upregulates fructolysis and glycolysis but inhibits pyruvate dehydrogenase. The forward metabolism of pyruvate is stopped. The dephosphorylation of phosphoenol pyruvate is inhibited in the setting of pyruvic kinase inhibition. Phosphoenol pyruvate enters the shikimic acid pathway where it is converted to chorismate. The shikimic acid is synthesized by a pathway starting from glyceraldehyde 3-phosphate. Glyceraldehyde 3-phosphate combines with the pentose phosphate pathway metabolite sedoheptulose 7-phosphate which is converted to erythrose 4-phosphate. The pentose phosphate pathway is upregulated in the presence of the suppression of glycolytic pathway. Erythrose 4-phosphate combines with phosphoenol pyruvate to generate shikimic acid. Shikimic acid combines with another molecule of phosphoenol pyruvate to generate chorismate. The chorismate is converted to prephenic acid and then to parahydroxy phenyl pyruvic acid. Parahydroxy phenyl pyruvic acid is converted to tyrosine and tryptophan as well as neuroactive alkaloids. The shikimic acid pathway is structured in expressed archaeaon organelle called the neurotransminoid. The fructolytic intermediates glyceraldehydes 3-phosphate and pyruvate are the starting points of the DXP pathway of cholesterol synthesis. Glyceraldehyde 3-phosphate combines with pyruvate to form 1-deoxy D-xylulose phosphate (DOXP) which is then converted to 2C methyl erythritol phosphate. 2C methyl erythritol phosphate can be synthesized from erythrose 4-phosphate a metabolite of the shikimic acid pathway. DXP combines with MEP to form isopentenyl pyrophosphate which is converted to cholesterol. Cholesterol is catabolised by archaeal cholesterol oxidases to generate digoxin. The digoxin sugars digitoxose and rhamnose are synthesized by the upregulated pentose

phosphate pathway. Glycolytic suppression leads to upregulation of the pentose phosphate pathway. The expressed archaeaon organelle concerned with cholesterol catabolism and digoxin synthesis is called the steroidelle. The suppression of glycolysis and stimulation of fructolysis results in upregulation of the hexosamine pathway. Fructose is converted to fructose 6-phosphate by ketohexokinases. The fructose 6-phosphate is converted to glucosamine 6-phosphate by the action of glutamine fructose 6-phosphate amidotransferase (GFAT). Glucosamine 6-phosphate is converted to UDP N-acetyl glucosamine which is then converted to N-acetyl glucosamine and various amino sugars. UDP glucose is converted to UDP D-glucuronic acid. UDP D-glucuronic acid is converted to glucuronic acid. This forms the uronic acid synthetic pathway. Uronic acids and hexosamines form repeating units of glycosaminoglycans. In the setting of glycolytic suppression and fructolytic metabolism fructolysis leads to increase synthesis of hexosamines and GAG synthesis. The GAG synthesizing archaeaon particles are called the glycosaminoglycoids. The expressed archaeaon particles are capable of synthesizing antioxidant vitamin C and E. The UDP D-glucose is converted to UDP D-glucuronic acid. UDP D-glucuronic acid is converted to D-glucuronic acid. D-glucuronic acid is converted to L-gulonate by enzyme aldoketoreductases. L-gulonate is converted to L-gulonolactone by lactonase. L-gulonolactone is converted to ascorbic acid by the action of archaeal L-gulo oxidase. The vitamin E is synthesized from shikimate which is converted to tyrosine and then to parahydroxy phenyl pyruvic acid. Parahydroxy phenyl pyruvic acid is converted to homogentisate. Homogentisate is converted to 2-methyl 6-phytyl benzoquinone which is converted to alpha tocopherol. 2-methyl 6-phytyl benzoquinone is converted to 2,3-methyl 6-phytyl benzoquinone and gamma tocopherol. Vitamin E can also be synthesized by the DXP pathway. Glyceraldehyde 3-phosphate and pyruvate combined to form 1-deoxy D-xylulose 5-phosphate which is converted to

3-isopentenyl pyrophosphate. 3-isopentenyl pyrophosphate and dimethyl allyl pyrophosphate combined to form 2-methyl 6-phytyl benzoquinone which is converted to tocopherols. The ubiquinone another important membrane antioxidant and part of the mitochondrial electron transport chain is synthesized by the shikimic acid pathway and DXP pathway. The isoprenoid moiety of ubiquinone is contributed from the DXP pathway and the rest of it by tyrosine catabolism. The tyrosine is generated by the shikimic acid pathway. The archaeaon particles concerned with the synthesis of vitamin C, vitamin E and ubiquinone which are all antioxidants are called the vitaminocyte.

Global warming induces endosymbiotic archaeal and RNA viroidal growth. The endosymbiotic archaea and the generated RNA viroids induce aldose reductase which converts glucose to sorbitol. The archaeal polysaccharides and lipopolysaccharides as well as viroids and viruses can induce aldose reductase. Sorbitol is acted upon by sorbitol dehydrogenase to generate fructose which enters fructolytic pathway. Aldose reductase is also induced by the osmotic stress of global warming and redox stress. Aldose reductase is induced by inflammatory and immune stimulation. Archaeal synthesized endogenous digoxin can produce intracellular redox stress and activate NFKB which produces immune activation. Both redox stress and immune activation can activate aldose reductase which converts glucose to fructose. Hypoxic stress or anerobic conditions induces HIF alpha which activates ketohexokinase C which phosphorylates fructose. Fructose is acted upon by fructokinase which converts fructose to fructose 1-phosphate. Fructose 1-phosphate is converted to dihydroxy acetone phosphate and glyceraldehydes 3-phosphate which is converted to pyruvate, acetyl CoA and citrate. Citrate is used for lipid synthesis. Fat deposition occurs in the visceral organs like the liver, heart and kidney. There is no subcutaneous fat deposit. Fructose metabolism bypasses phosphofructokinase which is inhibited by citrate and ATP. Fructose

metabolism is therefore not under the regulatory control of the enzyme phosphofructokinase. Fructose transport and metabolism is not regulated by insulin. Fructose is transported by glut-5 receptor. Fructose does not increase insulin secretion and therefore does not activate lipoprotein lipase. This results in visceral adipogenesis. Fructose induces ChREBP and SREBP elements. This results in increased hepatic lipogenesis by the induction of the enzyme fatty acid synthase, acetyl CoA carboxylase and steroyl CoA desaturace. This increases fatty acids and cholesterol synthesis. Fructose is a lipophilic carbohydrate. Fructose can be converted to glycerol 3-phosphate and fatty acids involved in triglyceride synthesis. Fructose administration leads to increase in triglycerides and VLDL. Fructose consumption leads to insulin resistance, fat accumulation in visceral organs like liver, heart and kidney, insulin resistance, dyslipidemia with increased triglycerides, VLDL and LDL as well as the metabolic syndrome. The metabolic syndrome X can be considered as a fructolytic syndrome. Fructose will increase lipid storage and promote insulin resistance. Fructose can fructosylate proteins producing dysfunction. Fructose has no effect upon ghrelin and leptin in the brain and can lead to increased feeding behaviour. Glucose decreases ghrelin and increases leptin levels. This leads to suppression of appetite. Thus fructose can modulate eating behaviour leading onto obesity. Fructose results in NFKB activation and TNF alpha secretion. TNF alpha can modulate the insulin receptor producing insulin resistance and metabolic syndrome X. Fructose can also lead to leptin resistance and obesity. There is an epidemic of metabolic syndrome X in relation to global warming.

Fructose can activate the sympathetic nervous system. This leads to hypertension and increase in heart rate. Fructose is involved in left ventricular hypertrophy, increase in left ventricular mass and decrease in left ventricular ejection fraction in hypertension. Fructose suppresses the parasympathetic nervous system. Fructose acts as a key inducer for uncontrolled proliferation and

hypertrophy of the cardiac musculature consequent to hypertension. The heart uses beta oxidation of fatty acids to generate energy. In the setting of anerobic glycolysis consequent to myocardial infarction and hypertensive hypertrophy of the heart, there is induction of HIF alpha. This produces increase in ketohexokinase C in the heart which phosphorylates fructose. Ketohexokinase C is a predominant liver enzyme as fructose metabolism is primarily focused in the liver. In the setting of anerobic glycolysis ketohexokinase C is also produced in the brain and the heart. Ketohexokinase A is the predominant enzyme in the heart and brain. In the setting of anerobic glycolysis ketohexokinase A which preferentially metabolizes glucose is converted to ketohexokinase C metabolizing fructose by the mechanism of RNA splicing. Anerobic conditions can induce HIF alpha which activates the splicing factor SF3B1. Thus HIF alpha induced by glycolysis induces SF3B1 which induces ketohexokinase C producing fructolysis in the heart. The fructose is converted to lipids, glycogen and glycosaminoglycans in the heart producing cardiac hypertrophy. Fructose metabolism is not under regulatory control of the key enzyme phosphofructokinase by citrate and ATP. The fructolytic pathway functions as a rogue pathway not under any regulatory control. Fructose is a key contributor. The sympathetic overactivity and parasympathetic blockade consequent to fructose can produce immune activation. The sympathetic overactivity and parasympathetic blockade can lead to dysregulation of the nervous system.

Fructose can activate NFKB and tumour necrosis factor alpha. The vagal blockade produced by fructose also leads to increase in immune activation. Fructose can inhibit neutrophilic phagocytosis. Increased fructose ingestion can lead to immune activation and respiratory diseases like chronic bronchitis, COPD and bronchial asthma as well as interstitial lung disease. This immune activation induced by fructose is called as fructositis. Fructosylated proteins can serve as autoantigens. Fructosylated proteins can bind to RAGE receptors

producing immune activation. Global warming induced fructose disease is the basis of the epidemic of autoimmune disease rising with the global warming.

Fructose increases flux through the pentose phosphate pathway. This increases the availability of hexose sugars like ribose for nucleic acid synthesis. This increases DNA synthesis. There is also consequent increase in protein synthesis. The tumour cells can slurp up fructose. Tumour cells utilise fructose for proliferation. The fetal cells like tumour cells also utilize fructose for proliferation. Fructose can promote metastatic deposits. The tumour cells use fructose differently from glucose. Cancer cells utilize fructose to support proliferation and metastasis. Fructose increases nucleic acid synthesis. Fructose can help the cancer cells to grow fast by inducing the transketolase enzyme and the pentose phosphate pathway. Fructose administration increases redox stress, DNA damage and cell inflammation all contributing to oncogenesis. Fructose is the most abundant sugar in the fetal tissues and is important in the development of fetus by promoting cell proliferation. Fructose is 20-times more concentrated in the fetal blood than glucose. Sperm cells and ova also use fructose for metabolism and energy. Thus all rapidly proliferating cells - cancer cells, fetal cells and reproductive cells depends upon fructolysis. Fructose is the principal diet of the cancer cells. Global warming and archaeal growth results in HIF alpha induction. HIF alpha induces tumour growth. HIF alpha also increases glycolysis. But archaeal induced HIF alpha also induces aldose reductase which converts glucose to fructose and metabolism proceeds along the fructolytic pathway. Fructosylation of glycolytic enzymes brings glycolysis to a halt. Fructosylation of mitochondrial PT pore hexokinase can result in PT pore dysfunction and cell proliferation. The fructolytic pathway is the principal energetic pathway for rapidly proliferating cancer cells, fetal cells and stem cells. The global warming will induce the Warburg phenotype of the fructolytic variety. This leads to an epidemic of cancer. There is an epidemic of cancer in

relation to global warming. The fructolytic pathway can lead to increased DNA synthesis and RNA synthesis due to flux via the pentose phosphate pathway. The fructolytic pathway can be directed to the GABA shunt generating succinyl CoA and glycine. These are substrates for porphyrin templates to form RNA viroids. The archaeal induced redox stress can induce endogenous HERV expression and reverse transcriptase expression. The RNA viroids are converted by HERV reverse transcriptase to corresponding DNA and integrated into the genome by HERV integrase. The integrated RNA viroid related DNA can function as jumping genes producing genomic plasticity and genomic change.

Fructose as said before induces the thiamine dependent transketolase flux. It increases both the oxidative and non oxidative pentose phosphate pathway. This increases nucleic acids and glycosaminoglycan synthesis. Fructose is converted to fructose 1-phosphate which is acted upon by aldolase B converting it into glyceraldehyde and dihydroxy acetone phosphate. Glyceraldehyde is converted glyceraldehyde 3-phosphate by triokinase. DHAP can be converted to glyceraldehyde 3-phosphate by the enzyme triose phosphate isomerase. Glyceraldehyde 3-phosphate can be converted to pyruvate. This pyruvate can be channeled to gluconeogenesis and glycogen storage by the action of the enzyme pyruvate carboxylase. This results in the conversion of glyceraldehyde 3-phosphate to pyruvate and via pyruvate carboxylase to glucose 1-phosphate. Glucose 1-phosphate is converted to glycogen polymers. Thus fructolysis results in glycogen storage. The pyruvate that is generated by fructolysis is converted to glutamate which can enter the GABA shunt pathway. The GABA shunt pathway generates glycine and succinyl CoA which are substrates for ALA synthesis. Thus fructolysis stimulates porphyrin synthesis. The porphyrins can self organize to form supramolecular arrays called porphyrions. Porphyrions can self replicate by using other porphyrions as templates. Porphyrions can have energetic and ATP synthesis by electron or photon transport. Porphyrions are dipolar molecules and

in the setting of digoxin induced membrane sodium potassium ATPase inhibition can generate a pumped phonon system induced quantal state and quantal perception. They can function as quantal computers with information storage. The porphyrions are basic self replicating living structures. The porphyrins can act as a template for the formation RNA, DNA and proteins. The RNA viroids, the DNA viroids and proteins generated by abiogenesis on porphyrin templates can self organize to form primitive archaea. The archaea are thus capable of abiogenic replication on porphyrin templates. The archaea can induce HIF alpha and further aldose reductase induction promoting fructolysis.

Fructose is an addictive substance. Fructose affects the hedonic centres in the brain concerned with pleasure and reward. In the addiction scale fructose is more addictive then cocaine and cannabis. Fructose decreases BDNF. Low BDNF produces changes in the brain resulting in schizophrenia and depression. Fructose can also produce chronic inflammation involved in schizophrenia. The fructolytic pathway is important in the genesis of psychiatric disorders. The increased fructolysis can lead to fructosylation of lipoproteins especially apoprotein E and apoprotein B. Apo B can undergo lysine fructosylation leading to defective LDL and cholesterol uptake by the brain. This results in autism and schizophrenia. Fructolysis leads to cholesterol depletion of the brain. Cholesterol is required for the formation of synaptic connections and cerebral cortex. This leads to cerebral cortical atrophy and cerebellar dominance in the presence of cholesterol depletion. This can contribute to the genesis of the cerebellar cognitive affective syndrome, the basis of schizophrenia and autism. There is an epidemic of schizophrenia and autism correlating with global warming. Fructosylation of LDL and brain cholesterol depletion can lead to dysfunction in synaptic transport. There is more release of glutamate into the synaptic from the presynaptic neuron consequent to a presynaptic neuron membrane dysfunction as a result of cholesterol depletion. This contributes to

glutamate excitotoxicity. Glutame excitotoxicity can contribute to neuronal degeneration. Fructose can also produce zinc deficiency. Increased fructose intake produces zinc depletion leading to defective formation of metallothionines leading to defective heavy metal excretion. This leads to mercury, cadmium and aluminium toxicity in the brain leading to psychiatric disorders like autism and degenerations like Alzheimer's disease. Zinc deficiency consequent to fructose excess can lead to copper excess. The zinc containing neurons in the cerebral cortex are called the gluzinergic neurons. The cerebral cortex especially the prefrontal cortex will atrophy producing cerebellar and brain stem dominance. Copper is required for the dominance of subcortical cognitive structures. Fructose ingestion can also lead to calcium deficiency which can produce defective calcium signaling. Fructose ingestion leads to fructolysis and the generation of reactive species 3-deoxyglucosone important in mallard reachion and fructosylation of neuronal proteins leading to their defective function. Neuropsychiatric disorders and neurodegenerative disorders can be described as fructose diseases. Topiramate a fructose analogue is used to treat motor neuron disease. Fructose biphosphate aldolase B mutation has been seen in schizophrenia, bipolar disorders and depression. 6-phosphofructo 2-kinase and fructose 2,6-biphosphotase abnormalities have been seen in schizophrenia. Fructose metabolism abnormalities have been noted in schizophrenia, manic depressive psychosis and autism. Fructose inhibits brain plasticity. Fructose inhibits the ability of neurons to communicate with each other. The wiring and re-wiring of neurons is inhibited. Fructose leads to a neuronal disconnection syndrome.

Fructose can increase flux via the pentose phosphate pathway and hexosamine pathway leading to glycosaminoglycan synthesis. Glycosaminoglycan accumulation in the tissues can produce mucopolysaccharidosis and fibrosis. Increased heparan sulphate accumulation in the brain leads to formation of

amyloids plaques and Alzheimer's disease. Connective tissue accumulation in the lung leads to interstitial lung disease, in the kidneys it produces tubular atrophy and a chronic renal failure similar to mesoamerican nephropathy. Connective tissue accumulation in the heart can lead to a restrictive cardiomyopathy. Accumulation of GAG especially hyaluronic acid in bones and joints leads to osteoarthritis and spondylosis. GAG accumulation in the endocrine organs can produce thyroid dysfunction resulting in MNG and thyroiditis, pancreatic dysfunction producing chronic calcific pancreatitis and adrenal dysfunction producing hypoadrenalism. Accumulation of GAG in the vascular tissues can result in mucoid angiopathy contributing to coronary artery disease and stroke. The accumulation of lipids due to the fructolytic pathway along with glycosaminoglycans can lead to fatty liver. This can later lead onto cirrhosis of the liver. Fructose is the principal culprit for fatty liver and cirrhosis. The glycine synthesized from the fructolytic intermediate phosphoglycerate can play a role inhibiting fatty liver. There is an epidemic of chronic renal failure due to tubular fibrosis, mucoid angiopathic vascular diseases, cardiomyopathy, multiple endocrine failures, cirrhosis of the liver, interstitial lung disease, degenerative bone and joint diseases and degenerative brain disease like Alzheimer's disease and Parkinson's disease as a consequence of global warming.

The increasing growth of archaea results in increased secretion of archaeal RNA viroids. They can interrupt mRNA function and dysregulates cell metabolism. This is by the mechanism of mRNA blockade. The viroidal RNA can combine with proteins generating prion proteins. This produces a protein conformation defect. This produces a prion protein disease. Abnormal protein conformation of beta amyloid, alpha synuclein, ribonuceloproteins, islet associated amyloid polypeptide and tumour suppressor protein can lead to an epidemic of Alzheimer's disease due to beta amyloid accumulation, alpha synuclein accumulation producing Parkinson's disease, prion like

ribonucleoproteins producing motor neuron disease, metabolic syndrome X due to defective insulin secretion as a result of IAPP and abnormal prion like tumour suppressor protein producing tumours. These prion diseases induced by archaeal RNA viroids are also transmissible. Thus global warming related fructolysis leads to archaeal induced RNA viroidal mediated prion disease and amyloidosis. This raises the spectacle of a Cassandra syndrome of human extinction.

Fructose is phosphorylated to fructose 1-phosphate by ketohexokinase C or fructokinase. Fructose 1-phosphate is converted to glyceraldehyde which is then converted to glyceraldehyde 3-phosphate and dihydroxy acetone phosphate (DHAP). Fructose 1-phosphate is cleaved to DHAP and glyceraldehyde 3-phosphate. DHAP can enter the glycolytic pathway or can go to gluconeogenetic pathway. DHAP generated from fructose 1-phosphate by the action of aldolase B is acted upon by triose phosphate isomerase converting it into glyceraldehydes 3-phosphate. Glyceraldehyde 3-phosphate can be fructolysed to pyruvate and acetyl CoA. Acetyl CoA can be used for cholesterol synthesis for storage. The pyruvate generated from glyceraldehydes 3-phosphate can be converted to the citrate which can be used for fatty acid synthesis by the action of enzymes acetyl CoA carboxylase, fatty acid synthase and malonate dehydrogenase. Glyceraldehyde is acted upon by alcohol dehydrogenase which converts it into glycerol. Glycerol is acted upon by glycerolkinase converting it into glycerol phosphate used for phosphoglyceride and triglyceride synthesis. Glyceraldehyde can also be acted upon by triokinase converting it into glyceraldehydes 3-phosphate which is then converted to DHAP by triose phosphate isomerase. Glyceral phosphate and dihydroxy acetone phosphate are interconvertible by the action of the enzyme glycerol phosphate dehydrogenase. Glycerol and fatty acids generated by fructolysis contribute to lipid synthesis and fat is stored. Fructose does not increase insulin secretion and doesn’t need insulin for transport into the cell. Fructose is

transported by the fructose transporter GLUT 5. Ketohexokinase C is exclusively seen in the liver which is the principal site of fructose metabolism. In the presence of hypoxia and anerobic states, there is induction of HIF alpha which can induce ketohexokinase C or fructokinase in the liver, kidney, gastrointestinal tract, brain and heart. Fructose 1-phosphate by-passes the enzyme phosphofructokinase which is the key regulatory enzyme the glycolytic pathway. Phosphofructokinase is inhibited by ATP and citrate. Thus stress induced fructolysis is an unregulated pathway not amenable to metabolic switches. Fructose does not depend upon insulin for its transport and fructolysis. Therefore fructolysis is not under insulin or endocrine control. It is an unregulated pathway.

The phosphorylation of fructose depletes the cell of ATP. Ketohexokinases preferentially phosphorylate fructose over glucose if it is available. In the presence of redox stress, osmotic stress and archaea/viroids aldose reductase is induced converting all the glucose to fructose. Glycolytic pathway comes to a halt as no ATP is available for phosphorylation of glucose and glucose as such gets converted to fructose. The fructose phosphorylation depletes the cell of ATP. ATP is converted to ADP and AMP which is deaminated to produce uric acid. Fructose increases flux in the pentose phosphate pathway increasing nucleic acid synthesis. Purine degradation results in hyperuricemia. Thus fructolysis results in increase in uric acid accumulation in the body. Uric acid will suppress the mitochondrial oxidative phosphorylation as well as produce endothelial dysfunction. The depletion of ATP by fructose phosphorylation results in membrane sodium potassium ATPase inhibition. This results in reduced energy needs of the cell as 80% of the ATP generated by metabolism is used for maintaining the sodium potassium pump. This results in membrane ATPase inhibition generated hibernatory state. The glyceraldehydes 3-phosphate generated by fructolysis can be converted to the pyruvate and

acetyl CoA used for cholesterol synthesis. The cholesterol that is synthesized is used for digoxin synthesis. Digoxin also has got aglycone part which contains sugars like digitoxose and rhamnose. Digitoxose and rhamnose are generated by the fructose induced flux and upgradation of the pentose phosphate pathway. Thus fructolysis results in a hyperdigoxinemic state and membrane sodium potassium ATPase inhibition. This results in cell protection and hibernation.

Fructose produces flux along the pentose phosphate pathway and hexosamine pathway. This results in GAG and nucleic acid synthesis. Fructose is converted to fructose 1-phosphate which is then converted to ribulose 5-phosphate. Ribulose 5-phosphate is acted upon by an isomerase converting it into xylulose 5-phosphate and ribose 5-phosphate. Xylulose 5-phosphate and ribose 5-phosphate interact to produce glyceraldehydes 3-phosphate and sedoheptulose 7-phosphate which is then converted to fructose 6-phosphate and erythrose 4-phosphate. The pentose phosphate pathway generates ribose for nucleic acid synthesis. The pathway also generates hexosamines for GAG synthesis. The pentose phosphate pathway also produces digitoxose and rhamnose for digoxin synthesis.

The global warming results in endosymbiotic archaeal growth. Archaea can induce aldose reductase which converts glucose to fructose. Fructolysis promotes flux along the pentose phosphate pathway generating nucleic acids and glycosaminoglycans. Fructolysis also generates glyceraldehydes 3-phosphate and further pyruvate. The pyruvate can enter the pyruvate carboxylase scheme generating gluconeogenesis and glycogen synthesis. Thus fructolysis can produce glycogen storage. Pyruvate can be converted to citrate for lipid synthesis. Pyruvate can also be converted to acetyl CoA for cholesterol synthesis. The flux along the pentose phosphate pathway generates the digoxin sugars, digitoxose and rhamnose. Cholesterol can be converted to digoxin

producing a hyperdigoxinemic state. Digoxin produces membrane sodium potassium ATPase inhibition. The selective phosphorylation of fructose by fructokinase depletes the cell of ATP producing membrane sodium potassium ATPase inhibition. This results in the generation of a hibernatory state. The fructolysis generated pyruvate can get converted to glutamate which can enter the GABA shunt pathway producing succinyl CoA and glycine for porphyrin synthesis. Porphyrins can form self replicating porphyrions or act as a template for the formation of RNA viroids, DNA viroids and prions which can symbiose to form archaea. Thus the archaea are capable of self replicating on porphyrin templates. The fructolysis thus produces a hibernatory syndrome with fat, glycogen and nucleic acid synthesis and storage. Fructolysis results in the generation of a hibernatory species, the homo neanderthalis. The fructolysis generated membrane sodium potassium ATPase inhibition results in cell hibernation and ATP sparing. The lack of ATP and digoxin induced membrane sodium potassium ATPase inhibition results in cortical inhibition and cerebellar dominance. This produces a somnolent state and a cerebellar cognitive affective disorder. The porphyrions generated by fructolysis produces quantal perception and cerebellar dominance. The storage of glycogen, fat and GAG results in obesity. The cerebellar cognitive affective syndrome results in a hypersexual state. The fructolysis and fructose can activate NFKB producing immune activation. The fructosylation of glycolytic and mitochondrial proteins suppresses the body's normal energetic which depends upon glycolysis and mitochondrial oxidative phosphorylation. Fructosylation of proteins results in blockade of glycolysis and mitochondrial oxidative phosphorylation. The body's energy needs are produced by fructolysis, porphyrin array mediated electron transport chain and ATP synthesis as well as membrane sodium potassium ATPase inhibition relation ATP synthesis. This produces a new species by archaeal symbiosis consequent to global warming - the homo

neanderthalis. This can be called as the tropical hibernatory syndrome consequent to global warming.

This can be called also as a fructose disease. Endosymbiotic archaea and viroids induce aldose reductase and converts body glucose to fructose leading to preferential fructose phosphorylation by ketohexokinase C. Fructolysis results in fructose 1-phosphate being acted upon by aldolase B resulting in the formation of glyceraldehyde and dihydroxy acetone phosphate. Glyceraldehyde can be converted to glyceraldehyde 3-phosphate and this contributes to pyruvate formation. Pyruvate enters the GABA shunt resulting in the formation of succinyl CoA and glycine. They are substrates for porphyrin synthesis and porphyrion formation. The porphyrins form a template for the formation of RNA viroids, DNA viroids, prions, isoprenoids and polysaccharides. They can symbiose together to form primitive archaea. The archaea can further induce HIF alpha, aldose reductose and fructolysis resulting in further porphyrinogenesis and archaeal self replication. The archaea by methanogenesis contributes to global warming which leads to further archaeal growth and a vicious cycle with no regulatory switches. The fructolytic pathway induced by archaea by-passes regulatory enzyme phosphofructokinase and is practically unregulated. Fructolytic pathway contributes to glycogen, lipids, cholesterol, hexose sugars and mucopolysaccharides synthesis and storage. This leads onto a hibernatory state and archaeal symbiosis induced species change resulting in neanderthalisation of the homo sapien species. The digoxin and fructose phosphorylation induced ATP depletion leads to membrane sodium potassium ATPase inhibition, sparing of ATP and tissue hibernation as most of the energy needs of the body are for the working of the sodium potassium pump. The cholesterol that is synthesized by fructolysis is catabolized cholesterol oxidases for archaeal energetics. Archaea also derives its energy from a primitive form of electron transport chain functioning in self replicating porphyrin arrays. The

archaeal digoxin induced sodium potassium ATPase inhibition can lead to membrane ATP synthesis. The archaea and the new human species phenotype derive its energy from the above mentioned mechanism. The glycolytic enzymes and the mitochondrial PT pore hexokinase are fructosylated making them dysfunction. The fructosylated glycolytic enzymes lead to generation of antiglycolytic enzyme antibodies and disease states. The human body's principal method of energetics tissue glycolysis and oxidative phosphorylation comes to a grinding halt. The human body is taken over by the overgrowth of endosymbiotic archaea and assumes hibernatory state with accumulation of glycogen, lipids, mucopolysaccharides and nucleic acids. The catabolic pathways for energy generation related to glucose, glycolysis and oxphos scheme stops. The human body can depend upon ketogenesis from fat and proteins. The upregulated fructolytic pathway generates phosphoglycerate which converted to phosphoserine and glycine. They can be converted to other amino acids and used for ketogenesis. The body assumes a high BMI index and obesity with visceral fat storage and adiposity akin to the Neanderthal metabolic phenotype. Digoxin induced membrane sodium potassium ATPase inhibition results in cortical dysfunction. The brain porphyrins can form a quantal pumped phonon system resulting in quantal perception and low level EMF absorption. This leads to prefrontal cortex atrophy and cerebellar dominance. Fructose itself leads to sympathetic hyperactivity and parasympathetic blockade. This leads onto a functional form of cerebellar cognition and quantal perception resulting in a new brain phenotype. The cerebellar cognitive syndrome leads to a robotic human phenotype. The phenotype is impulsive, has extrasensory perception and has less of speech production. Communication is by symbolic acts. The cerebellar phenotype doesn't have a cortical control and contributes to surrealistic behavior patterns. This produces impulsive behavior and an epidemic of surrealism where the rational prefrontal cortex becomes extinct.

This leads to extremes of spirituality, violent and terroristic behavior and hypersexual states contributing to a state of trancedence underlined and reinforced by quantal perception. Cerebellar phenotype owing to its quantal perception behaves as a community and not as an individual. This creates new social and psychological phenotypes. Fructose induces NFKB and immune activation. This results in an immune activatory phenotype. Cultured T-reg cells on high fructose diet have 62% less IL-40 secretion than controls. This results in a hyperimmune state with fructosylated proteins acting as antigens. The fructolytic pathway can lead to increased DNA synthesis and RNA synthesis due to flux via the pentose phosphate pathway. The fructolytic pathway can be directed to the GABA shunt generating succinyl CoA and glycine. These are substrates for porphyrin templates to form RNA viroids. The archaeal induced redox stress can induce endogenous HERV expression and reverse transcriptase expression. The RNA viroids are converted by HERV reverse transcriptase to corresponding DNA and integrated into the genome by HERV integrase. The integrated RNA viroid related DNA can function as jumping genes producing genomic plasticity and genomic change. This produces a new genotype. Fructosylation of body proteins and enzymes results in a protein processing defect resulting in loss of protein function. The human cell function due to protein fructosylation, protein processing defects and protein conformational defects comes to a grinding halt. Fructolytic pathway generates porphyrin arrays induced ATP production, membrane sodium potassium ATPase inhibition induced ATP synthesis and fructolysis induced ATP generation. This provides energy for porphyrin template induced archaeal replication. The digoxin and fructose phosphorylation induced ATP depletion produces cell membrane sodium potassium ATPase inhibition and a hibernatory state. This leads onto a somnolent sleepy state. The cholesterol catabolism by cholesterol oxidases for archaeal energetics leads to defective sex hormone synthesis. This leads onto an

asexual androgynous state. The cerebellar cognitive syndrome due to prefrontal cortical atrophy consequent to porphyrion induced low level EMF perception produces a hypersexual state. This results in male-female equidominance and changes in sexual behavior of the population. Thus the fructose disease consequent to global warming results in a new neuronal, immune, metabolic, sexual, social phenotype. The human body is converted to a zombie for the global warming related endosymbiotic archaea to thrive. The neuronal, metabolic, sexual and social phenotype creates the necessary environment endosymbiotic archaeal multiplication and the human body is converted to a zombie phenotype. This can be called as a hibernatory zombie syndrome. Due to the new sexual and social phenotype with asexuality and hypersexuality and female-male equidominance the human population falls. The global warming and archaeal induction of HIF alpha resulting in the Warburg phenotype leads to changes in the metabolic scheme of the cells producing body cell transformation to stem cells. The stem cells depend upon glycolysis or fructolysis for energy needs. The Warburg phenotype produces an acidic pH which can result in conversion of body cells to stem cells. The stem cells conversion results in loss of tissue function. The cerebral cortex synaptic connectivity is lost and becomes dysfunction leading to subcortical cerebellar dominance. The immune stem cells proliferate producing an autoimmune disease. The various tissue cells the specialized function like neuron, nephron and muscle cell all because of stem cell conversion becomes dysfunctional. This produces a stem cell syndrome with human somatic cells being converted to stem cells with loss of function and uncontrolled proliferation. The fructosylation of proteins results in protein function defects. The fructosylation of LDL results in defective cholesterol transport to the cells. This results in steroidal hormone synthesis defects. Cholesterol is required for formation of synaptic connectivity and this leads to cerebral cortical dysfunction. The hemoglobin becomes fructosylated and

oxygen transport is affected. This leads to hypoxia and anerobic states. The hypoxia and anerobic states induces HIF alpha and the Warburg fructolytic phenotype. The HIF alpha also induces aldose reductase converting glucose to fructose and inducing the fructolytic scheme. The fructolysis induced GABA shunt pathway and porphyrin synthesis results in further archaeal porphyrin template related replication. This results in further archaeal induced fructolysis and the vicious irreversible cycle proceeds. The uncontrolled growth of archaea leads to still further global warming. The world of endosymbiotic eternal archaea takes over and persists during the extremophilic climatic changes of global warming. The human beings exist as neanderthalic zombies serving archaeal multiplication. The homo sapiens gets converted to a new phenotype, genotype, immunotype, metabolonomic type and brain type. This is called as hibernatory zombie related to global warming - homo neoneanderthalis.

Table 1

	Serum fructose		**Serum fructokinase**		**Aldolase B**		**Total GAG**	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	2.50	0.195	8.50	0.405	3.50	1.304	3.50	0.707
EMF	30.79	4.740	21.47	3.056	11.65	1.427	20.54	2.192
CCP	31.16	3.635	22.42	3.126	10.49	1.476	17.94	2.276
MNG	32.24	5.864	20.46	2.864	9.82	1.135	21.42	2.662
Muc ANG	30.40	6.405	23.30	4.089	11.08	1.360	22.16	3.543
F value	17.373		13.973		13.903		21.081	
p value	< 0.01		< 0.01		< 0.01		< 0.01	

Table 2

	Total TG		**Serum ATP levels**		**Uric acid**		**Anti-aldolase**	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	124.00	3.688	2.50	0.405	5.70	0.369	7.50	1.704
EMF	270.10	28.792	0.81	0.079	8.76	0.881	1.31	0.329
CCP	293.00	28.111	0.78	0.145	8.30	0.966	1.31	0.265
MNG	262.70	30.324	0.83	0.091	8.04	0.667	1.55	0.493
Muc ANG	275.40	30.351	0.77	0.138	8.83	0.633	1.47	0.466
F value	16.378		59.169		14.166		55.173	
p value	< 0.01		< 0.01		< 0.01		< 0.01	

Table 3

	Anti-enolase		**Anti-pyruvatekinase**		**Anti-GAPDH**	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	1.50	0.358	50.40	5.960	5.20	0.363
EMF	0.42	0.182	14.55	3.133	1.24	0.239
CCP	0.50	0.149	17.82	2.889	1.44	0.234
MNG	0.47	0.151	17.59	2.469	1.44	0.270
Muc ANG	0.36	0.114	18.63	3.147	1.48	0.271
F value	14.091		21.073		58.769	
p value	< 0.01		< 0.01		< 0.01	

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2

Endemic Hyperdigoxinemia Related Cardiovascular and Endocrine Mucopolysaccharidoses Syndrome

Introduction

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

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

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

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

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

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

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

Kerala has a high incidence of endomyocardial fibrosis (EMF), chronic calcific pancreatitis (CCP), multinodular goitre (MNG) and mucoid angiopathic lesions presenting as coronary artery disease and thrombotic strokes. EMF claims 2.5% of all cardiac patients under 40 years who attend hospitals in Kerala. Kerala has the highest incidence of tropical pancreatitis in India. From 1980-1986 it accounted for 0.2% of total admissions and 7% of all diabetic admissions to the Trivandrum Medical College Hospital. MNG accounts for nearly 1.5% of total admissions in this hospital every year. Sandhyamoni has demonstrated a high incidence of mucoid angiopathic lesions in autopsy studies of the coronary and cerebral vessels with acid mucopolysaccharides

accumulating in the tunica intima and media. There is magnesium deficiency in cardiac tissues of EMF patients. Magnesium deficiency is also a risk factor in the development of diabetes mellitus. In this context it has been reported that there are elevated levels of a hypothalamic archaeal endogenous membrane sodium potassium ATPase inhibitor, digoxin in the serum of diabetic patients. Membrane sodium potassium ATPase inhibition can lead to magnesium deficiency. Hypomagnesemia has been reported to produce upregulation of GAG synthesis in experimental models. Alteration in connective tissue metabolism may underlie EMF, CCP, MNG and mucoid angiopathy which are known to coexist in the very same geographic zone. Elevated digoxin levels and hypomagnesemia are known to contribute to insulin resistance. It has been reported that there is a high incidence of insulin resistance and metabolic syndrome X in Asian populations inhabiting the very same endemic zone.

Global warming leads to dehydration and osmotic stress. Global warming also leads to increased actinidic archaeal growth. Archaea catabolizes cholesterol and synthesizes digoxin. Digoxin can inhibit sodium potassium ATPase and increase intracellular calcium load producing mitochondrial PT pore dysfunction. This leads to oxidative stress. Osmotic stress and oxidative stress can induce the enzyme aldose reductase which converts glucose to fructose. Fructose has got a low km value for ketokinase as compared to glucose. Therefore fructose gets selectively phosphorylated to fructose phosphate which can be converted to glucosamine and galactosamine. Thus aldose reductase inhibition consequent to osmotic and oxidative stress of global warming can induce glycosaminoglycan synthesis. This study was undertaken to assess the following parameters in EMF, CCP, MNG and mucoid aniopathy-serum magnesium, serum total GAG, serum levels of various GAG fractions and serum digoxin levels. A hypothesis highlighting the pivotal role of endogenous digoxin in the pathogenesis of these disorders, which could be different spectra

of a common insulin resistance state is also presented. This can lead to a global warming related Lemurian cardiovascular and endocrine syndrome.

Materials and Methods

Informed consent was obtained from all the patients as well as relatives of subjects included in the study. Necessary ethical clearance was also obtained for this study from the ethical committee of the Medical College Hospital, Trivandrum. Fifteen cases of EMF, CCP, MNG and mucoid angiopathic strokes and CAD from Department of Medicine, Cardiology and Gastroenterology of Medical College Hospital, Trivandrum were chosen for the study. The patients aged 25-50 years were selected randomly over a period of 2 years as and when they were admitted to the wards. They were all freshly diagnosed cases and fasting blood was removed from them before any treatment was started as was from the equal number of age and sex matched healthy controls. The healthy normal controls were selected randomly from the general population of the Trivandrum district. Autopsy samples of heart tissue from EMF patients were supplied by the Sree Chitra Tirunal Institute for Medical Sciences and Technology. Autopsy samples of thyroid tissue from MNG cases were obtained from the Department of Pathology, Medical College Hospital, Trivandrum and autopsy samples of pancreatic tissue from chronic calcific pancreatitis patients were supplied by the Diagnostic and Research Centre, Trivandrum. Carotid arteries and aortic specimens with histopathologically demonstrated mucoid angiopathy were obtained from the Department of Forensic Pathology, Medical College, Alleppey. For comparison cardiac, thyroid, pancreas, aortic and carotid tissue from accident subjects (25-50 yrs.) were used and these were also obtained from the Department of Forensic Pathology, Medical College, Alleppey. Concentration of total GAG and various GAG fractions were determined by methods described earlier. The tissue GAG was extracted by

Folch's procedure. The dry defatted tissue was digested with papain and GAG was estimated as described before. Total cholesterol, HDL cholesterol and triglycerides were estimated in the serum by enzymatic methods. The kits were supplied by M/s Sigma Chemicals, USA. Serum magnesium was determined by atomic absorption spectrophotometry. RBC membrane for estimation of sodium potassium ATPase was prepared according to the procedure of Blostein. For estimation of sodium potassium ATPase activity of the erythrocyte membrane, the procedure described by Wallach and Kamat was used. Digoxin in the serum was determined by the procedure by Wallah and Kamat was used. Digoxin in the serum was determined by the procedure described by Wallah and Kamat was used. Digoxin in the serum was determined by the procedure described by HPLC. Statistical analysis was carried out by ANOVA.

Results

1. Lipid profile of patients with EMF, CCP, MNG and mucoid angiopathy showed normal serum LDL cholesterol, low serum HDL cholesterol, elevated serum triglycerides and normal total serum cholesterol
2. Serum magnesium was decreased in patients with EMF, CCP, MNG and mucoid angiopathy
3. Serum total GAG was elevated in patients with EMF, CCP, MNG and mucoid angiopathy
4. The individual serum GAG fractions showed the following patterns in mucoid angiopathy - ChS forming 76.19% followed by DS forming 10% of GAG. The other fractions - HA, HS and H are present only in small amounts
5. Tissue total GAG was elevated in patients with EMF, CCP, MNG and mucoid angiopathy

6. RBC membrane sodium potassium ATPase activity was reduced in patients with EMF, CCP, MNG and mucoid angiopathy.
7. Serum digoxin level was elevated in patients with EMF, CCP, MNG and mucoid angiopathy.

Discussion

Archaeal Digoxin and Membrane Na^+-K^+ ATPase Inhibition in Relation to EMF, CCP, MNG and Mucoid Angiopathy

The archaeaon steroidelle DXP pathway and the upregulated pentose phosphate pathway contribute to digoxin synthesis. Endogenous digoxin like activity (EDLA) has been reported in several pathological conditions by reaction with digoxin antibodies. We have recently shown that the EDLA is in the fact due to the steroidal glycoside, digoxin itself. Endogenous digoxin which is reported to be synthesized by the hypothalamus and other tissues, is a potent inhibitor of membrane sodium potassium ATPase. It is also reported that several plant sources contain digoxin like steroidal glycosides and the vegetarian diet consumed by populations in this geographic zone may be a rich source for digoxin. The increase in digoxin levels in the serum of these patients may therefore be due to increased endogenous synthesis and/or that derived from dietary sources. The decrease in membrane sodium-potassium ATPase activity in the patients of CCP, EMF, MNG and mucoid angiopathy may be due to this increase in digoxin levels. The inhibition of membrane sodium potassium ATPase by digoxin is known to cause an increase in intracellular calcium resulting from increased sodium calcium exchange, increased entry of calcium via the voltage gated calcium channel and increased release of calcium from intracellular endoplasmic reticulum calcium stores. This increase in intracellular calcium by displacing magnesium from its biding sites causes a decrease in the

functional availability of magnesium. The decrease in the availability of magnesium can cause decreased mitochondrial ATP formation which along with low magnesium can cause further inhibition of membrane sodium potassium ATPase, since the ATP-magnesium complex is the actual substrate for this reaction. Cytosolic free calcium is normally buffered by two mechanisms, ATP dependent calcium extrusion from the cell and ATP dependent sequestration of calcium within the endoplasmic reticulum. The magnesium related mitochondrial dysfunction results in defective calcium extrusion from the cell. There is thus a progressive inhibition of membrane sodium-potassium ATPase activity first triggered by digoxin. Low intracellular magnesium and high intracellular calcium consequent to membrane sodium potassium ATPase inhibition appear to be crucial to the pathophysiology of these disorders. Membrane sodium potassium ATPase inhibition could in part be contributed to by the low level of background irradiation from the mineral sands in Kerala coast which produces membrane disruption. Earlier it was postulated that the cerium from the mineral sands is ingested and is exchanged for magnesium leading to magnesium depletion had postulated a protein deficiency model for this group of disorders. But there is no nutritional data to support any but marginal protein deficiency in the Kerala population. It is interesting to note that intracellular magnesium deficiency can produce ribosomal disruption and inhibition of protein synthesis. Therefore protein deficiency could be a functional correlate of magnesium depletion. The population of Kerala consumes a high carbohydrate and high fibre diet. The total dietary fibre intake is around 20 g per day. Fibre has been reported to bind to magnesium producing magnesium depletion via the stools. Cyanide from dietary sources has also been implicated in the etiology of this group of disorders. Cyanide can produce inhibition of cytochrome oxidase and produce a mitochondrial dysfunction leading to ATP depletion and membrane

sodium-potassium ATPase inhibition. Serum magnesium was assessed in all these disorders and was found to be reduced.

Archaeal Digoxin and Mitochondrial Dysfunction in Relation to EMF, CCP, MNG and Mucoid Angiopathy

The archaeaon vitaminocyte contributes to the synthesis of ubiquinone and mitochondrial electron transport chain function. The mitochondrial function related free radical generation is regulated by the archaeaon vitaminocyte synthesized tocopherol and ascorbic acid. Increased calcium within the cell can open the mitochondrial PT pore, disrupt the inner membrane hydrogen gradient and uncouple oxidative phosphorylation. This results in volume dysregulation of the mitochondrial matrix, hyperosmolality of the matrix, outer membrane rupture and release of cyto C and AIF (apoptosis inducing factor) into the cytosol. This activates procaspase-9 to caspase-9 which produces apoptosis and replacement fibrosis.

Archaeal Digoxin and Regulation of Golgi Body / Lysosomal Function in Relation to EMF, CCP, MNG and Mucoid Angiopathy

The archaeaon glycosaminoglycoid and fructosoid contributes to glycoconjugate synthesis and catabolism by the process of fructolysis. The intracellular magnesium depletion related inhibition of glycolysis, citric acid cycle and oxidative phosphorylation can channel more glucose-6 phosphate for the synthesis of GAG precursors. Magnesium deficiency in fact has been shown by us to result in glycosaminoglycan accumulation in tissues. Glycosaminoglycan accumulation has been described in these disorders, which can be explained as being due to magnesium deficiency. Decrease in intracellular magnesium can result in a glycosylation defect since magnesium is a cofactor for formation of dolichol-1 phosphate required for N-glycosylation

and nucleoside diphosphate sugars required for O-glycosylation. The defective glycoproteins may be responsible for micro and macroangiopathy of diabetes mellitus in CCP. Defectively processed N-glycosylated glycoproteins can also lead on to a defective insulin sensing mechanism of the beta cells. Intracellular magnesium deficiency can lead to upregulation of GAG synthesis and their accumulation in the pancreatic tissues. MPS accumulation in the pancreas has been described in CCP.

Archaeal Digoxin and Insulin Resistance

Increase in beta cell calcium can contribute to increased insulin release from beta cells and hyperinsulinemia. Hypomagnesemia has been reported to markedly increase glucose stimulated insulin secretion by the perfused pancreas. Magnesium deficiency can also lead to insulin resistance. Magnesium translocation appears to be an early event in insulin action. Decrease in intracellular magnesium can block the phosphorylation reactions involved in protein tyrosine kinase receptor activity leading to insulin resistance. Elevated fibre content of the diet can also mimic the action of insulin leading to hyperinsulinism. On the other hand magnesium deficiency produced by dietary fibre can lead to insulin resistance. Insulin administration has been reported to lead to an upregulation of GAG synthesis. The lipid profile of the patient with EMF, MNG, CCP and mucoid angiopathy is similar to that obtained in the insulin resistance state. It is tempting to speculate that all these diverse group of disorders are due to insulin resistance.

Increase in intracellular calcium can activate the G-protein coupled signal transduction system of the contra-insulin hormones - glucagon, adrenaline, noradrenaline and the growth hormone via the growth hormone releasing factor. This results in increased production of glucose. Decrease in intracellular magnesium can lead to inhibition of glycolysis causing defective glucose

utilization and hyperglycemia. Increase in intracellular calcium can open up the mitochondrial PT pore, disrupt the hydrogen gradient across the inner membrane and block mitochondrial oxidative phosphorylation. Intracellular magnesium deficiency can also lead to a ATP synthase defect. All this leads to defective glucose utilization and hyperglycemia. As already described above increased intracellular calcium and reduced intracellular magnesium can lead to hyperinsulinism and insulin resistance described in CCP.

Archaeal Digoxin, Immune Activation and CCP

Again the increased intracellular calcium can activate the T-cells via the calcium dependent calcineurin pathway producing an increase in TNF alpha secretion. This results in immune activation and the inflammatory changes noticed in the pancreas and other tissues especially peripheral nerve in CCP. Increase in TNF alpha secretion. This results in immune activation and the inflammatory changes noticed in the pancreas and other tissues especially peripheral nerve in CCP. Increase in TNF alpha can also contribute to insulin resistance.

Archaeal Digoxin and Thyroid Dysfunction

The intracellular deficiency of magnesium, which is required for protein transcription and translation, results in a nuclear and ribosomal dysfunction. The thyroid hormone receptor belongs to the steroid receptor family and has a DNA binding site. The intracellular magnesium deficiency results in a thyroid hormone receptor defect. This results in defective feed back inhibition to the hypothalamus and pituitary and increased TRH and TSH secretion. There is also increased activity of TSH and TRH owing to increased intracellular calcium and increased G-protein coupled signal transduction of these hormones. The multinodular goitre arises owing to TSH dependent thyroid proliferation. The

inhibition of sodium potassium ATPase produces inhibition of the sodium potassium ATPase coupled neutral amino acid tyrosine transport into the thyroid follicular cell. The iodide transport into the thyroid follicular cell also depends on ATP. The intracellular magnesium depletion produces defective ATP synthesis and a mitochondrial dysfunction in the thyroid follicular cell. This results in defective iodide transport into the cell. Defective iodide and tyrosine transport into the cell can produce defects in thyroid hormone synthesis and the resulting hypothyroidism can lead on to increased TSH levels. The depleted intracellular magnesium can stimulate mucopolysaccharide biosynthesis and fibrosis of the thyroid gland. MPS accumulation has been demonstrated in the thyroid tissue in MNG.

Archaeal Digoxin and Regulation of Cell Division, Cell Proliferation and Neoplastic Transformation in Relation to CCP and MNG - Relation to Immune Activation

The archaeaon fructosoid contributes to fructolysis and immune activation. Fructose can contribute to induction of NFKB and immune activation. The archaeaon steroidelle synthesized digoxin induces NFKB producing immune activation. CCP and MNG are precancerous states. CCP has been found to lead to carcinoma of the pancreas and multinodular goitre is a predisposing factor for thyroid malignancies. Membrane sodium potassium ATPase inhibition can lead to oncogenesis. Intracellular calcium activates phospholipase C beta which results in increased production of diacylglycerol (DAG) with resultant activation of protein kinase C. The protein kinase C (PKC) activates the MAP kinase cascade resulting in cellular proliferation. The decreased intracellular magnesium can produce dysfunction of GTPase activity of the alpha-subunit of G protein. This results in RAS oncogene activation, as more of the RAS is bound to GTP rather than GDP. Phosphorylation mechanisms are required for the activation of the tumour

suppressor gene P_{53}. The activation of P_{53} is impaired owing to intracellular magnesium deficiency producing a phosphorylation defect.

Archaeal Digoxin and Endomyocardial Fibrosis

Membrane sodium potassium ATPase inhibition can produce a decrease in the intramyocardial cell magnesium and an increase in the intramyocardial cell calcium. The increase in intramyocardial cell calcium can open the mitochondrial PT pore, destroy the hydrogen gradient across the inner membrane and uncouple oxidative phosphorylation. The decrease in intramyocardial cell magnesium can inhibit ATP synthase and produce a defective mitochondrial oxidative phosphorylation. This results in a myocardial mitochondrial dysfunction and increased generation of free radicals due to incomplete reduction of molecular oxygen. Free radicals can produce damage to myocardium. The opening of the mitochondrial PT pore can produce osmotic dysregulation and hyperosmolality of the mitochondria, rupture the outer mitochondrial membrane and release AIF (apoptosis inducing factor) and cyto C in to the cytosol. This activates procaspase-9 to caspase-9 producing myocardial apoptosis and replacement fibrosis. The decrease in intracellular magnesium can result in increased channelling of glucose 6-phosphate to the synthesis of GAG precursors and increased glycosaminoglycan biosynthesis. Decrease in intracellular magnesium can produce changes in collagen and elastin biosynthesis and result in replacement fibrosis. MPS accumulation has been demonstrated in EMF tissues by previous studies. The increase in intracellular calcium can produce T-cell activation via the calcium dependent calcineurin pathway releasing TNF alpha, from the activated T-cell. Elevated levels of TNF alpha have been related to myocardial dysfunction. Impairment of calcium homeostasis, decrease in magnesium ATPase activity and troponin I phosphorylation, cytokine expression especially TNF alpha and aberrant

induction of apoptosis have been described in cardiomyopathies. The basic defect in cardiomyopathy is thus interstitial/endocardial fibrosis and MPS/elastin deposition which can occur in magnesium deficiency. Increase in intracellular calcium can activate the G protein coupled signal transduction system of the platelet activating factor and thrombin. Magnesium deficiency can produce increased platelet aggregation and release reaction and thrombosis resulting in the formation of a LV or RV thrombus which can get fibrosed leading on to endocardial fibrosis.

Archaeal Digoxin and Mucoid Angiopathy

Membrane sodium-potassium ATPase inhibition induced hypomagnesemia related increased glycosaminoglycan synthesis can contribute to mucoid angiopathy. Increased intracellular calcium within the endothelial cell leads to fragmentation of the elastic membrane and calcification. Increased calcium within the arterial wall alters elastin synthesis, turnover and composition. Increase in arterial wall cellular calcium can open the mitochondrial PT pore, produce osmotic dysregulation and hyperosmolality of the mitochondrial matrix, rupture the outer membrane and release cyto C and AIF to the cytosol producing vascular wall cellular apoptosis. In mucoid angiopathy there is a uniform hose pipe like narrowing of large, medium sized and small sized arteries with deposition of acidic mucopolysaccharides in the tunica intima and media. Increase in intracellular calcium can activate the G-protein coupled thrombin receptor and platelet activating factor producing the thrombosis observed in mucoid angiopathy. Decreased intracellular magnesium can lead to increased thrombin and ADP/collagen induced platelet aggregation. Membrane sodium potassium ATPase inhibition related increased smooth muscle calcium and decreased magnesium can contribute to the vasospasm and ischaemia observed in mucoid angiopathic, stroke and CAD. Decreased intracellular

magnesium can produce dysfunction of lipoprotein lipase producing defective catabolism of triglycerides rich lipoproteins and hypertriglyceridemia. In hypomagnesemia, lecithin cholesterol acyl transferase (LCAT) is defective and there is reduced formation of cholesterol esters in HDL. This results in reduced HDL cholesterol levels described in mucoid angiopathy. The increase in intracellular calcium can activate phospholipase A_2 producing increased amounts of arachidonic acid for thromboxane A_2 synthesis via the cyclooxygenase pathway. This can lead on to increased platelet aggregation and thrombosis in mucoid angiopathy.

Archaeal Digoxin Related Endemic Mucopolysaccharidotic Syndrome

MNG, CCP, EMF and mucoid angiopathy belong to the same geoendemic zone. The study shows that they share the same etiological factors of causation.

1. Low membrane sodium potassium ATPase and magnesium depletion consequent to increased digoxin from exogenous or endogenous sources
2. Hypomagnesemia related elevated GAG synthesis
3. Digoxin induced hypomagnesemia related insulin resistance state/hyperinsulinism producing elevated GAG synthesis.

Therefore these disorders could be termed as the endemic hyperdigoxinemia related cardiovascular and endocrine mucopolysaccharidoses syndrome. Global warming leads to dehydration and osmotic stress. Global warming also leads to increased actinidic archaeal growth. Archaea catabolizes cholesterol and synthesizes digoxin. Digoxin can inhibit sodium potassium ATPase and increase intracellular calcium load producing mitochondrial PT pore dysfunction. This leads to oxidative stress. Osmotic stress and oxidative stress can induce the enzyme aldose reductase which converts glucose to fructose.

Fructose has got a low km value for ketokinase as compared to glucose. Therefore fructose gets selectively phosphorylated to fructose phosphate which can be converted to glucosamine and galactosamine. Thus aldose reductase inhibition consequent to osmotic and oxidative stress of global warming can induce glycosaminoglycan synthesis. The fructose phosphorylation depletes the cell of ATP. This results in inhibition of glucose phosphorylation, glycolysis and mitochondrial oxidative phosphorylation. The depletion of cellular ATP results in oxidative stress. Oxidative stress can open the mitochondrial PT pore, release cytochrome c and activate the caspase cascade of cell death. Oxidative stress generated by cellular depletion of ATP consequent to fructose phosphorylation and digoxin induced mitochondrial dysfunction can produce further aldose reductase induction. This results in more conversion of glucose to fructose. The fructose can produce mitochondrial dysfunction on its own. The fructose can also fructosylate proteins making them antigenic and the oxidative stress induced by fructose phosphorylation and depletion of cellular ATP can activate NFKB producing immune activation. The fructose phosphate can get converted to glucosamine and galactosamine increasing GAG synthesis. This results in increase in heparan sulphate which can combine with proteins producing amyloidosis. Thus the cell death, glycosaminoglycan synthesis, amyloidogenesis, immune activation and autoimmunity produced by fructosemia or fructositis can contribute to mucoid angiopathy, endomyocardial fibrosis, chronic calcific pancreatitis and multinodular goitre. This can be called a global warming related mucopolysaccharidotic syndrome.

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The Actinidic Archaea Related Lemurian Syndrome - Endomyocardial Fibrosis, Chronic Calcific Pancreatitis, Multinodular Goitre and Mucoid Angiopathy

Introduction

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

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

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

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

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

Actinidic beach sands have been postulated to play a pivotal role in abiogenesis. Chronic calcific pancreatitis (CCP), endomyocardial fibrosis (EMF), multinodular goitre (MNG) and mucoid angiopathy along with the root

wilt disease of coconut is endemic to Kerala with its radioactive actinide beach sands. The Actinides like rutile producing intracellular magnesium deficiency due to actinide-magnesium exchange sites in the cell membrane has been implicated in the etiology of EMF.[1-3] Endogenous digoxin, a steroidal glycoside which functions as a membrane sodium-potassium ATPase inhibitor has also been related to its etiology of EMF, CCP, MNG and mucoid angiopathy.[4] Digoxin produces intracellular magnesium deficiency which results in acidic mucopolysaccharide accumulation of the vascular, cardiac and endocrine tissues contributing to the pathogenesis. Organisms like phytoplasmas and viroids have also been demonstrated to play a role in the etiology of root wilt disease of coconut which is co-endemic in Kerala.[5, 6] The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered.[7-9] The role of RNA viroids in the etiopathogenesis of EMF, CCP, MNG and mucoid angiopathy was also explored. Davies has put forward the concept of a shadow biosphere of organisms with alternate biochemistry present in earth itself.[10] An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described.[7]

The group of diseases are seen in particular geographic areas of the world near the equator - South India, South America, South Africa and Australia.[1-3] These geographic areas are rich in placer deposits containing monazite, illmenite, rutile and thorium. These areas peninsular India, Africa, Australia, South America and Antarctica formed part of one single pre-historic continent in Southern ocean and Indian Ocean called Lemuria by geologists. The evolution of primates and homo sapiens occurred in the rift valley of Africa part of this pre-historic continent. Metal actinides in beach sands have been postulated to play a role in abiogenesis. Actinide mineral like rutile, monazite and illmenite by surface metabolism would have contributed to abiogenesis. 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. Actinide dependent organism would have contributed to primate and human evolution. It is also possible that actinidic organisms would also have contributed to the destruction of the Lemurian supercontinent. This paper postulates that the co-existence of EMF, CCP and MNG in the above mentioned geographic areas points to the possibility of these land masses being joined together has one single land mass - Lemuria.

Actinidic archaea has been related to global warming and human diseases. The growth of endosymbiotic actinidic archaea in relation to climate change and global warming leads to neanderthalisation of the humans. Neanderthal metabolonomics include the Warburg phenotype and cholesterol catabolism resulting in hyperdigoxinemia. Digoxin produced by archaeal cholesterol catabolism produces neanderthalisation. The neanderthalisation of the human brain due to endosymbiotic archaeal overgrowth results in prefrontal cortical atrophy and cerebellar hyperplasia. This leads on to dysautonomia with sympathetic hyperactivity and parasympathetic neuropathy in these disorders.

Global warming can lead to osmotic stress consequent to dehydration. The increase in actinidic archaeal growth leads to cholesterol catabolism and digoxin synthesis. Digoxin produces membrane sodium potassium ATPase inhibition and increase in intracellular calcium producing mitochondrial dysfunction. This results in oxidative stress. The oxidative stress and osmotic stress can induce the enzyme aldose reductase which converts glucose to fructose. Fructose has got a low km value for ketokinase as compared to glucose. Therefore fructose gets phosphorylated more to fructose phosphate and the cell is depleted of ATP. The cell depletion of ATP leads to oxidative stress and chronic inflammation

consequent to induction of NFKB. Oxidative stress can open the mitochondrial PT pore producing release of cyto C and activation of the caspase cascade of cell death. The fructose phosphate can enter the pentose phosphate pathway synthesizing ribose and nucleic acid. The depletion of cellular ATP results in generation of AMP and ADP which are acted upon by deaminases causing hyperuricemia. Uric acid can produce endothelial dysfunction and vascular disease. Uric acid can also produce mitochondrial dysfunction. The fructose phosphate can enter the glucosamine pathway synthesizing GAG and producing mucopolysaccharide accumulation. Fructose can fructosylate proteins making them antigenic and producing an autoimmune response. This can lead to the global warming related Lemurian syndrome of EMF, CCP, MNG and mucoid angiopathy.

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, chronic calcific pancreatitis, multinodular goitre and mucoid angiopathy. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond.[11] 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 urease.[12-15] 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 urease. 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 % (Increase without Doxy)		Muramic acid % (Decrease with Doxy)		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
Muc Angio	24.43	0.81	68.72	2.77	24.32	1.09	65.80	5.14
EMF	22.28	1.52	64.05	2.79	22.82	1.56	64.61	4.95
CCP	23.07	1.46	64.68	3.86	22.89	1.50	64.19	6.51
MNG	23.85	1.69	66.43	3.17	22.72	1.64	63.91	4.93
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
Muc Angio	22.27	1.49	63.99	4.03	22.27	1.49	69.25	2.33
EMF	22.29	2.05	58.70	7.34	22.29	2.05	67.03	5.97
CCP	21.19	2.18	61.63	7.68	21.19	2.18	62.99	5.47
MNG	22.93	2.08	63.49	5.01	23.19	1.74	65.68	4.06
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
Muc Angio	24.44	0.90	59.90	4.74	23.90	1.36	63.29	6.86
EMF	22.92	1.48	61.91	7.56	23.73	1.38	65.20	6.20
CCP	23.27	1.96	63.09	9.21	22.85	1.71	66.14	3.58
MNG	23.65	1.88	64.78	6.62	23.79	1.19	64.24	3.96
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 urease.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		Urease % change (Increase with Rutile)		Urease % 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
Muc Angio	0.53	0.03	0.224	0.041	23.37	1.55	63.99	4.03
EMF	0.51	0.05	0.213	0.033	23.41	1.41	58.70	7.34
CCP	0.47	0.05	0.212	0.028	22.44	2.00	61.63	7.68
MNG	0.51	0.06	0.227	0.040	22.15	1.79	65.49	7.28
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
Muc Angio	22.27	1.49	61.94	5.49	23.67	1.65	69.25	2.33
EMF	22.29	2.05	62.37	5.05	21.66	1.94	67.03	5.97
CCP	21.19	2.18	54.82	8.70	22.27	2.18	62.99	5.47
MNG	19.73	2.27	59.36	7.53	22.51	2.32	62.70	3.24
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
Muc Angio	23.64	1.50	60.44	6.83	22.27	1.49	59.90	4.74
EMF	23.29	1.67	60.52	5.38	22.29	2.05	61.91	7.56
CCP	23.38	1.79	57.37	7.45	21.19	2.18	63.09	9.21
MNG	22.00	1.77	61.39	7.47	22.71	1.82	66.13	3.83
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
Muc Angio	23.45	1.52	67.05	4.84	23.72	1.76	58.92	5.46
EMF	23.37	1.31	63.97	3.62	22.70	1.87	60.46	8.06
CCP	22.53	1.92	66.31	3.10	21.31	1.37	57.32	8.41
MNG	23.39	1.14	68.11	3.02	22.17	2.01	65.15	6.46
F value	449.503		673.081		306.749		130.054	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Abbreviations

Muc Angio: Mucoid angiopathy

EMF: Endomyocardial fibrosis

CCP: Chronic calcific pancreatitis

MNG: Multinodular goitre

Discussion

Archaeal Cholesterol Catabolism in Relation to EMF, CCP, MNG and Mucoid Angiopathy

The archaeaon steroidelle DXP pathway and the upregulated pentose phosphate pathway contribute to digoxin synthesis. There was increase in cytochrome F420 indicating archaeal growth in endomyocardial fibrosis, chronic calcific pancreatitis, multinodular goitre and mucoid angiopathy. The archaea can synthesise and use cholesterol as a carbon and energy source.[16, 17] 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.[18] There was also an increase in archaeal HMG CoA reductase activity indicating increased cholesterol synthesis by the archaeal mevalonate pathway. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis and archaeal cholesterol hydroxylase activity indicating bile acid synthesis were increased.[8] The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide.[17] 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.[19] The archaeal glycolytic hexokinase activity and archaeal extracellular ATP synthase activity were increased.

Archaeal-Viroidal Human Genomic Sequences in Relation to EMF, CCP, MNG and Mucoid Angiopathy

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.[20] 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.[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 and changing DNA sequences. The RNA viroids can regulate mRNA function by RNA interference.[20] The phenomena of RNA interference can modulate euchromatin / heterochromatin expression. RNA viroidal mRNA interference plays a role in the pathogenesis of endomyocardial fibrosis, chronic calcific pancreatitis, multinodular goitre and mucoid angiopathy. The viroidal RNA modulation of T-cell and B-cell function by mRNA interference can lead to immune activation. Monocytic infiltration of the vascular wall, cardiac and endocrine tissue can produce reactive connective tissue macromolecular deposition contributing to EMF, CCP, MNG and mucoid angiopathy. The viroidal RNA mediated mRNA interference can also inhibit insulin signalling and secretion leading onto CCP. The viroid RNA can inhibit thyroid hormone secretion and action by mRNA interference leading to increased TSH secretion and multinodular goitre.

Actinidic Nanoarchaea and Secreted RNA Viroids in Relation to EMF, CCP, MNG and Mucoid Angiopathy

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.[24] 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.[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 synthesised PAH and methane leading on to redox stress. Redox stress leads to sodium potassium ATPase inhibition, inward movement of plasma membrane cholesterol, defective SREBP sensing, increased cholesterol synthesis and nanoarchaeal / mevalonate pathway bacterial growth.[29] Redox stress leads on to viroidal and archaeal multiplication. Redox stress can also lead to HERV reverse transcriptase and integrase expression. The noncoding DNA is formed of integrating RNA viroidal complementary DNA and archaea with the integration going on as a continuing event. The change in the length and grammar of the noncoding region produces eukaryotic speciation and

individuality.[30] Thus actinidic nanoarchaea would have contributed to the evolution of the multicellular eukaryote, primates and humans. Changes in the length of noncoding region especially due to integration of viroid complementary DNA and archaea and the resulting jumping genes leads to new DNA sequences possibly contributing to EMF, CCP, MNG and mucoid angiopathy.[31] 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. Archaea and mevalonate pathway bacteria can lead onto EMF, CCP, MNG and mucoid angiopathy. The persistent symbiosis leads to reparative connective tissue macromolecular deposition of acidic mucopolysaccharides, glycoproteins, collagen and elastin leading to fibrotic changes in the heart, vessel wall, thyroid and pancreas contributing to EMF, CCP, MNG and mucoid angiopathy.[4, 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 metabolic and immune phenotype or microchimeras leading on to human diseases like EMF, CCP, MNG and mucoid angiopathy with a predilection to develop malignancy. Microchimeras can lead to cellular polyploidy important in malignant transformation and induction of carcinoma of thyroid and pancreas. The growth of archaea in the vascular, cardiac and endocrine tissues can result in calcification. The archaea can form calcified nanoarchaeal structures which can exist as colonies in slime. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms.[33] The calcified

nanoarchaea can contribute to the tissue calcification noted in CCP, MNG and mucoid angiopathy.

Archaea and RNA Viroids Related Immune Activation and Connective Tissue Deposition Contributing to EMF, CCP, MNG and Mucoid Angiopathy

Archaea and RNA viroid can bind the TLR receptor induce NFKB producing immune activation and cytokine TNF alpha secretion. The archaeal DXP and mevalonate pathway metabolites can bind γδ TCR and digoxin induced calcium signalling can activate NFKB producing chronic immune activation.[4, 34] The archaea and viroid can induce chronic immune activation and generation of superantigens. The archaea and viroid induced chronic immune activation can lead to monocyte infiltration of the vessel wall, cardiac and endocrine tissues leading on to reparative connective tissue macromolecular deposition. Immune activation results in induction of NADPH oxidase which generates hydrogen peroxide. Cholesterol oxidase activity also generates hydrogen peroxide. Hydrogen peroxide can produce tissue injury in MNG, CCP, EMF and mucoid angiopathy contributing to reparative connective tissue macromolecular deposition. Immune activation can also produce insulin resistance. TNF alpha produced by chronic immune activation can modulate the insulin receptor producing insulin resistance.[35] Chronic immune activation and cholesterol oxidase generated hydrogen peroxide can induce neutral sphingomyelinase generating ceramide producing insulin resistance.[36] This can contribute to chronic calcific pancreatitis. Immune activation and NFKB induction can suppress the thyroid hormone receptor resulting in hypothyroidism and increased TSH levels contributing to thyroid gland enlargement and multinodular goitre. Immune activation and NFKB induction can suppress the nuclear receptors LXR, PXR and FXR. FXR suppression can also lead to

insulin resistance as well as increased connective tissue MPS deposition in vessel wall, cardiac tissue and endocrine tissue. LXR suppression by NFKB stimulates HMG CoA reductase activity and suppresses cholesterol 7-alpha hydroxylase activity.[37] This stimulates cholesterol synthesis and inhibits its degradation via the bile acid pathway. PXR suppression by NFKB prevents cholesterol detoxification via the bile acid shunt pathway.[38] Thus LXR and PXR suppression by NFKB produces acute cholesterol toxicity. The increased cholesterol in the system leads to still further archaeal multiplication and growth as they depend on cholesterol as a carbon and energy source.

Actinidic Archaea and RNA Viroids Induce the Warburg Phenotype Contributing to EMF, CCP, MNG and Mucoid Angiopathy

Archaea, viroids and digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype.[39] 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. Mitochondrial dysfunction owing to the Warburg's phenotype can contribute to ineffective glucose utilisation and CCP. 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.[39] The increased cholesterol substrate also leads to increased archaeal growth and digoxin synthesis due to metabolic channelling to the mevalonate pathway. The Warburg phenotype leads to increased lipid synthesis and defective beta oxidation of fatty acids. The myocardium depends on fatty acids beta oxidation for energetics. The defective beta oxidation of fatty acids leads to myocardial dysfunction and EMF. The Warburg phenotype leads to upregulated glycolysis

and increase in the metabolite fructose 1,6-diphosphate which is channelled to the pentose phosphate pathway. This can generate UDP sugars used for mucopolysaccharide synthesis. This results in acidic MPS deposition in the tissues leading onto EMF, CCP, MNG and mucoid angiopathy. The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy needs. Ammonia can stimulate membrane sodium-potassium ATPase, increase ATP utilisation and produce mitochondrial transmembrane potential changes leading to mitochondrial dysfunction. This causes defective glucose utilisation contributing to CCP. Archaeal urease can convert urea to ammonia and thiocyanate. Increase cyanide load in the system can lead to mitochondrial dysfunction.[3] Cyanide related mitochondrial dysfunction can produce EMF, CCP and MNG. It produces defective cardiac function, decreased glucose utilisation and impaired iodide transport into the thyroid follicular cells. The Warburg phenotype can also lead onto malignant transformation. The upregulated glycolysis results in increased mitochondrial PT pore hexokinase and cell proliferation producing carcinoma of thyroid and pancreas.

Archaea and Viroid Induced Endocrine and Cardiovascular Mucopolysaccharidotic Syndrome

Digoxin can produce sodium-potassium ATPase inhibition and inward movement of plasma membrane cholesterol. This produces defective SREBP sensing, increased HMG CoA reductase activity and cholesterol synthesis.[29] The digoxin induced inward movement of plasma membrane cholesterol can alter membrane cholesterol / sphingomyelin ratio producing modified lipid microdomains.[40] The digoxin induced lipid microdomain modulation can regulate the GPCR couple adrenaline, noradrenaline, glucagon and neuropeptide receptors as well as protein tyrosine kinase linked insulin receptor. This can lead onto CCP. The digoxin mediated inhibition of nuclear membrane

sodium-potassium ATPase can modulate nuclear membrane lipid microdomains and thyroxine DNA receptor function. This can lead onto hypothyroidism, increased TSH levels and thyroid gland enlargement contributing to MNG. Digoxin can produce intracellular hypercalcemia and hypomagnesemia. This can lead on to vasospasm and thrombosis. Intracellular hypercalcemia can activate the G-protein coupled thrombin receptor and PAF receptor producing thrombosis. Intracellular magnesium deficiency can lead onto increased thrombin and ADP/collagen induced platelet aggregation. This leads onto the thrombotic state in mucoid angiopathy. The decreased intracellular magnesium can produce ATP synthase inhibition and the increased intracellular calcium can produce mitochondrial PT pore dysfunction. Mitochondrial dysfunction can contribute to decreased glucose utilisation in CCP and myocardial dysfunction in EMF. Digoxin can produce sodium-potassium ATPase inhibition and intracellular hypomagnesemia. The increased tissue rutile load can lead to rutile-magnesium exchange leading onto intracellular hypomagnesemia. Hypomagnesemia can lead onto upregulated connective tissue macromolecular synthesis contributing to MNG, CCP, EMF and mucoid angiopathy. Acidic MPS deposition in the vessel wall leads to a hose pipe narrowing of the entire vascular tree leading onto mucoid angiopathy. Acidic MPS, collagen and elastin deposition of the heart leads to EMF. Hyperdigoxinemia is important in the pathogenesis of EMF, CCP, MNG and mucoid angiopathy. Digoxin induced sodium-potassium ATPase inhibition results in an ATP sparing effect.[41] Eighty percent of the ATP generated is used to run the sodium-potassium ATPase pump. The digoxin inhibition of the sodium-potassium ATPase spares this ATP which is then used for lipid and cholesterol synthesis. Fat also fuels insulin resistance by binding to the toll receptor and producing immune activation and immune infiltration of the adipose tissue. Digoxin can also increase lymphocytic intracellular calcium

which leads on to induction of NFKB and immune activation.[4] The archaeal cholesterol catabolism can deplete the lymphocytic cell membranes of cholesterol resulting in alteration of lymphocytic cell membrane microdomains related receptors producing immune activation, monocytic infiltration and reparative connective tissue macromolecular deposition.

NMDA can be activated by digoxin induced calcium oscillations, PAH and viroid induced RNA interference.[4] The cholesterol ring oxidase generated pyruvate can be converted by the GABA shunt pathway to glutamate. Glutamatergic transmission can lead to immune activation. Immune activation can lead to reparative connective tissue macromolecular deposition in EMF, CCP, MNG and mucoid angiopathy. The cholesterol aromatase generated serotonin is well known to produce connective tissue macromolecule especially collagen deposition producing the fibrotic changes in EMF, mucoid angiopathy, MNG and CCP. The archaeal cholesterol aromatase can generate PAH.[19] The PAH can also lead to insulin resistance and CCP. PAH can also inhibit thyroid hormone receptor function contributing to hypothyroidism, increased TSH, thyroid enlargement and MNG. Particulate pollution has been related to vascular thrombosis and can lead to mucoid angiopathy. PAH particles are also known to produce myocardial dysfunction. Thus the actinide, viroid and mevalonate pathway bacteria induced metabolic, genetic, immune and neuronal transmission changes can lead onto endemic EMF, CCP, MNG and mucoid angiopathy. The term archaea and viroid induced endemic cardiovascular and endocrine mucopolysaccharidoses can be used to describe this entity.

Actinidic Archaea in the Kerala Coast May Be Abiogenetic Precursors of Life

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.[42] 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 a evolutionary advantage and the symbiosis of archaea with gram negative organism generated the eukaryotic cell.[43] 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. The presence of placer deposits and mineral sands containing monazite, illmenite, rutile and thorium in the Lemurian supercontinent would have made it the ideal place for the primitive cell, nanoarchaea, eukaryote, multicellular eukaryote, primates and humans to evolve. Anthropological studies have provided evidence for the evolution of primates and homo sapiens in the rift valley of Kenya part of the prehistoric Lemurian continent.

Global Warming, Fructolysis and Mucopolysaccharidotic Syndrome

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

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

Actinidic Archaea in the Interstellar Space and the Biological Universe

The archaea can synthesise magnetite by biomineralisation. The archaeal cholesterol catabolism can generate PAH. The archaea can exist as nanoarchaea and can have calcified nanoforms. The actinidic magnetotactic nanoarchaea and its secreted PAH organisms are extremophiles and survive in the interstellar space and can contribute to the interstellar grains and magnetic fields which play a role in the formation of the galaxies and star systems.[44] The cosmic dust grains occupy the intergalactic space and are thought to be formed of magnetotactic bacteria identified according to their spectral signatures.

According to the Hoyle's hypothesis, the cosmic dust magnetotactic bacteria play a role in the formation of the intergalactic magnetic field. A magnetic field equal in strength to about one millionth part of the magnetic field of earth exists throughout much of our galaxy. The magnetic files can be used to trace the spiral arms of the galaxy following a pattern of field lines that connect young stars and dust in which new stars are formed at a rapid rate. Studies have shown that a fraction of the dust particles have elongated shape similar to bacilli and they are systematically lined up in our galaxy. Moreover the direction of alignment is such that the long axes of the dust tend to be at right angles to the direction of the galactic magnetic field at every point. Magnetotactic bacteria have the property to affect the degree of alignment that is observed. The fact that the magnetotactic bacteria appear to be connected to the magnetic field lines that thread through the spiral arms of the galaxy connecting one region of star formation to another support a role for them in star formation and in the mass distribution and rotation of stars. The nutrient supply for a population of interstellar bacteria comes from mass flows out of supernovas populating the galaxy. Giants arising in the evolution of such stars experience a phenomenon in which material containing nitrogen, carbon monoxide, hydrogen, helium, water and trace elements essential for life flows continuously outward into space. The interstellar bacteria need liquid water. Water exists only as vapour or solid in the interstellar space and only through star formation leading to associated planets and cometary bodies can there be access to liquid water. To control conditions leading to star formation is of paramount importance in cosmic biology. The rate of star formation is controlled by two factors: Too high a rate of star formation produces a destructive effect of UV radiation and destroys cosmic biology. Star formation as stated before produces water crucial for bacterial growth. Cosmic biology of magnetotactic bacteria and star formation are thus closely interlinked. Systems like solar systems do not arise in

random condensation of blobs of interstellar gas. Only by a rigorous control of rotation of various parts of the system would galaxies and solar system evolved. The key to maintaining control over rotation seems to lie in the intergalactic magnetic field as indeed the whole phenomena of star formation. The intergalactic magnetic fields owes its origin to the lining up of magnetotactic bacteria and the cosmic biology of interstellar bacteria can prosper only by maintaining a firm grip on the interstellar magnetic field and hence on the rate of star formation and type of star system produced. This points to a cosmic intelligence or brain capable of computation, analysis and exploration of the universe at large - of magnetotactic bacterial networks. The origin of life on earth according to the Hoyle's hypothesis would be by seeding of bacteria from the outer intergalactic space. Comets carrying microorganisms would have interacted with the earth. A thin skin of graphitized material around a single bacteria or clumps of bacteria can shield the interior from destruction by UV light. The sudden surge and diversification of species of plants and animals and their equally sudden extinction has seen from fossil records point to sporadic evolution produced by induction of fresh cometary genes with the arrival of each major new crop of comets.[45, 46] The interstellar PAH aromatic organism is formed from nanoarchaeal cholesterol catabolism. The PAH and cholesterol are the interconvertible primal prebiotic molecules. PAH aromatic organism and nanoarchaeal magnetite can have a wave particle existence and bridge the world of bosons and fermions. The nanoarchaea can form biofilms and the PAH aromatic organism can form a molecular quantum computing cloud in the biofilm which forms a interstellar intelligence regulating the formation of star systems and galaxies. The magnetite loaded nanoarchaeal biofilms and PAH aromatic organism quantal computing cloud can bridge the wave particle world functioning as the anthropic observer sensing gravity which orchestrates the reduction of the quantal world of possibilities in to the macroscopic world. The

actinide based nanoarchaea can regulate the earth's carbon cycle by methanogenesis, nitrogen cycle by ammonia oxidation and rain formation by contributing the seeding nucleus. The earth's temperature and global warming and cooling are regulated by nanoarchaeal synthesised PAH from cholesterol and methanogenesis. The increased nanoarchaeal growth in ocean beds and soil leads to increased methane production and movement of the earth's crust producing tsunamis and massive earthquake leading to catastrophic mass extinction.[47] This nanoarchaeal growth in the Southern ocean and Indian Ocean bed due to global warming induced by civilisational progress and human activity would have led to methane burps in the ocean bed contributing to massive earthquakes leading onto Tsunamis. This would have led to catastrophic destruction of the Lemurian supercontinent. The migration of the Lemurian survivors into the Indian subcontinent Indus valley, the Nile valley and the Mesopotamian valley would have contributed to the origin of the Harappan, Sumerian and Egyptian civilization which have all evolved during the same period of human history.[48, 49] The eternal nanoarchaea survive and start the cycle of evolution once more. The actinide based nanoarchaea regulates the human system and biological universe.

Actinidic Archaea and the Lemurian Syndrome

The coexistence of EMF, CCP and MNG in South India, South Africa, Australia and South America is thus an indirect evidence for the existence of the Lemurian supercontinent containing these land masses. The actinidic nanoarcheal growth would have led to methane burps in the ocean bed contributing to earthquakes and Tsunamis producing extinction of the Lemurian supercontinent. It also supports the abiogenesis on radioactive actinidic beach sands through the process of surface metabolism. This gives support to the role of actinidic archaea as the third element that controls life and its role in the

evolution of the multicellular eukaryote, primates and humans. Civilization and humans would have evolved in the placer deposits and actinidic sand rich pre-historic Lemurian supercontinent in the Indian and Southern ocean.[48, 49]

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