GLOBAL WARMING

Archaea and Viroid Induced Symbiotic Evolution of Homo Sapiens and Homo Neanderthalis – Archaeal RNA Viroidal Quasi-Species Consortia and Human Species Identity - The Neoneanderthal Age and Kali Yuga

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Chapter 1

The Endosymbiotic Archaea, Fructose Disease, Digoxin Syndrome and Global Warming - Relation to Human Species - Homo Sapiens and Homo Neanderthalis

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.

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. The archaeal symbiosis leads to the evolution of a new human neoneanderthal species. This can be called as the neoneanderthal age or Kali yuga.

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 bye-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. The colonic and endosymbiotic archaea and other microbes like clostridial clusters determine the species, race, caste, community and personal identity of the individual. The identity of the individual - personal, community, caste, race, nationality and species is determined by the colonic and endosymbiotic archaeal and clostridial clusters. Predominent archaeal symbiosis produces homo neanderthalis and less prominent archaeal symbiosis and dominant clostridial clusters in the gut produces the homo sapien species. Each individual, race, nationality, caste, creed and community have the endosymbiotic and colonic microbiota signature. This colonic and endosymbiotic microbiota signature is transferable by the change of endosymbiotic and colonic microbiota from one group to another. Thus the evolution and identity based on individuality, race, nationality, caste and creed can be induced.

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 archaeal population densities and quasi-species RNA viroidal networks determine homo sapien, homo neanderthalis, racial, caste, community, national, sexual and individual identity.

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 civilization - 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 human brain can be considered as a modified archaeaon colony network. The archaeaon are eternal and can last for billions of years. The human brain is basically an information storage system. The archaeaon has got dipolar magnetite and porphyrins and can function as quantal computer. The archaeal colony with its dipolar magnetite and porphyrin in the setting of archaeal digoxin induced membrane sodium potassium ATPase inhibition can function as a pumped phonon system mediating quantal perception. The archaeaon in the brain is capable of information storage at a point in time and space. The experiences and information stored in the archaeaon is immortal and eternal. The archaeaon can have a wave particle existence and can exist in multiple quantal possible states and can inhabit multiple quantal multiverses. The interaction between information stored in quantal computers in multiple different archaeaon systems all over the universe by the quantal interactions results in eternal existence of information in quantal multiverses. The information in the quantal multiverses can have a particulate existence creating a newer mode by quantal interactions between information stored at multiple points of time. This creates the particulate mythic world of human existence. These are what are called as Samsaras. The mind is uploaded into information in the neuronal archaeal colony network and its quantal computers. The information stored in the archaeal colony network mediated quantal state is eternal and can be considered as a digital version of the brain, a mind downloading technique or whole brain emulation. The archaeal colony network stores the human experiences in an eternal manner and can contribute to biological reincarnation.

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 2-C methyl erythritol phosphate. 2-C methyl erythritol phosphate can be synthesized from erythrose 4-phosphate a metabolite of the shikimic acid pathway. DXP combines with MEP to form isopentenyl pyrophosphate which is converted to cholesterol. Cholesterol is catabolized by archaeal cholesterol oxidases to generate digoxin. The digoxin sugars digitoxose and rhamnose are synthesized by the upregulated pentose phosphate pathway. Glycolytic suppression leads to upregulation of the pentose phosphate pathway. The expressed archaeaon organelle concerned with cholesterol catabolism and digoxin synthesis is called the steroidelle. The suppression of glycolysis and stimulation of fructolysis results in upregulation of the hexosamine pathway. Fructose is converted to fructose 6-phosphate by ketohexokinases. The fructose 6-phosphate is converted to glucosamine 6-phosphate by the action of glutamine fructose 6-phosphate amidotransferase (GFAT). Glucosamine 6-phosphate is converted to UDP N-acetyl glucosamine which is then converted to N-acetyl glucosamine and various amino sugars.

UDP glucose is converted to UDP D-glucuronic acid. UDP D-glucuronic acid is converted to glucuronic acid. This forms the uronic acid synthetic pathway. Uronic acids and hexosamines form repeating units of glycosaminoglycans. In the setting of glycolytic suppression and fructolytic metabolism fructolysis leads to increase synthesis of hexosamines and GAG synthesis. The GAG synthesizing archaeaon particles are called the glycosaminoglycoids. The expressed archaeaon particles are capable of synthesizing antioxidant vitamin C and E. The UDP D-glucose is converted to UDP D-glucuronic acid. UDP D-glucuronic acid is converted to D-glucuronic acid. D-glucuronic acid is converted to L-gulonate by enzyme aldoketo reductases. 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 adipogeneis. 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 stearoyl 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 coverted 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, ribonucleoproteins, 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 percent 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 and 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	8.5	0.405	3.50	1.304	3.50	0.707
Sy X	21.20	5.201	18.91	2.942	8.01	1.244	18.46	4.623
CAD	31.40	3.212	21.18	2.267	9.02	0.667	21.41	1.653
CVA	29.98	4.002	24.96	3.829	11.72	1.397	21.65	2.755
DCM/EMF	32.04	4.955	21.37	2.050	10.89	1.344	20.12	2.855
Tumour	27.94	3.732	22.29	1.237	9.46	1.386	20.89	1.651
Schizo	31.14	4.446	22.19	2.634	11.63	3.081	21.50	1.714
Autism	28.66	5.089	24.09	2.146	12.30	1.621	22.60	3.054
AD	33.13	2.754	19.87	1.646	11.37	1.406	22.97	3.662
PD	30.24	4.551	22.72	1.955	11.93	2.999	20.13	1.507
MS	29.88	5.150	22.29	1.641	10.87	1.895	23.47	2.878
Lupus	33.11	4.509	20.24	1.639	11.59	0.767	20.62	3.504
CRF	30.24	3.209	22.52	3.196	11.76	1.596	20.55	2.164
ILD	32.04	5.295	22.37	1.585	11.84	0.963	21.49	1.544
COPD	26.68	4.266	21.78	2.253	10.62	1.703	22.84	2.965
BA	33.59	3.938	22.45	2.472	11.30	0.783	23.50	3.225
Cirrhosis	32.53	6.737	23.00	1.722	10.49	1.373	20.57	1.878
IBD	31.75	5.236	21.89	2.292	11.63	1.304	22.46	4.030
MAO	31.53	4.507	22.07	2.324	11.32	1.343	23.89	2.936
IBS	29.90	4.299	22.52	1.995	10.93	1.498	22.09	2.797
PUD	32.49	6.487	21.89	3.431	10.85	1.606	25.27	3.693
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
DBJD	33.06	5.970	22.42	3.714	11.21	1.660	17.76	3.556
Spondylosis	32.70	4.430	21.92	1.840	14.10	2.423	26.80	3.679
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
Sy X	262.40	32.790	0.82	0.143	6.21	0.452	2.20	0.583
CAD	252.44	35.388	0.85	0.085	9.00	0.485	2.23	0.567
CVA	297.64	36.410	0.79	0.081	9.34	1.641	2.02	0.303
DCM/EMF	302.00	25.166	0.77	0.151	9.26	1.048	1.41	0.310
Tumour	277.60	34.613	0.80	0.136	7.88	0.847	1.45	0.415
Schizo	244.00	31.383	0.72	0.102	8.65	0.701	1.35	0.319
Autism	284.30	19.743	0.87	0.072	8.14	0.538	1.35	0.218
AD	244.70	22.106	0.82	0.121	8.74	0.687	1.70	0.361
PD	284.30	19.945	0.83	0.090	8.90	0.579	2.03	0.232
MS	289.89	23.406	0.74	0.115	9.59	0.783	1.80	0.402
Lupus	294.00	39.903	0.78	0.161	8.34	0.712	1.81	0.691
CRF	272.10	31.057	0.86	0.101	7.76	0.798	1.67	0.363
ILD	292.10	26.337	0.78	0.135	8.40	0.442	1.72	0.360
COPD	306.40	24.419	0.74	0.136	9.62	0.952	1.63	0.440
BA	293.80	31.555	0.72	0.134	9.51	1.059	2.10	0.572
Cirrhosis	271.80	37.818	0.79	0.150	8.12	0.747	1.67	0.377
IBD	287.50	20.414	0.77	0.102	9.44	0.924	1.30	0.223
MAO	316.20	31.283	0.76	0.103	9.32	0.864	1.41	0.307
IBS	279.10	27.606	0.77	0.095	9.68	1.060	1.44	0.350
PUD	285.70	22.628	0.76	0.126	9.77	0.957	1.14	0.134
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
DBJD	282.60	27.573	0.79	0.136	8.28	0.978	1.89	0.315
Spondylosis	295.30	16.600	0.72	0.108	10.21	1.310	1.54	0.377
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
Sy X	0.51	0.185	17.04	3.556	1.73	0.371
CAD	0.55	0.154	16.06	6.811	1.78	0.349
CVA	0.66	0.182	21.79	4.567	1.50	0.307
DCM/EMF	0.49	0.197	18.68	4.585	1.54	0.471
Tumour	0.42	0.182	19.93	2.421	1.39	0.253
Schizo	0.40	0.142	22.02	11.954	1.31	0.235
Autism	0.20	0.060	19.27	2.201	1.20	0.205
AD	0.38	0.205	18.87	3.899	1.37	0.305
PD	0.42	0.208	20.11	3.220	1.44	0.342
MS	0.39	0.124	18.93	6.447	1.78	0.355
Lupus	0.42	0.116	18.59	3.721	1.48	0.258
CRF	0.55	0.220	17.06	3.449	1.32	0.358
ILD	0.52	0.202	18.80	3.221	1.41	0.355
COPD	0.59	0.159	18.14	3.500	1.71	0.509
BA	0.36	0.177	15.33	3.212	1.72	0.277
Cirrhosis	0.48	0.273	18.60	2.915	1.52	0.287
IBD	0.43	0.163	17.06	4.366	1.40	0.298
MAO	0.44	0.230	19.08	3.396	1.48	0.220
IBS	0.57	0.242	19.99	2.637	1.39	0.289
PUD	0.51	0.221	20.63	5.116	1.42	0.329
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
DBJD	0.54	0.211	22.48	4.638	1.33	0.302
Spondylosis	0.40	0.134	19.91	5.099	1.49	0.282
F value	14.091		21.073		58.769	
p value	< 0.01		< 0.01		< 0.01	

Refernces

[1] Kurup RK, Kurup PA. *Global Warming, Archaea and Viroid Induced Symbiotic Human Evolution and the Fructosoid Organelle*. New York: Open Science, 2016.

Chapter 2

Hyperdigoxinemic Right Hemispheric Dominant Familial Cluster - Digoxin Excess Syndrome - The Homo Neanderthalis Family

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 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. The archaeal symbiosis leads to the evolution of a new human neoneanderthal species. This can be called as the neoneanderthal age or Kali yuga.

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 bye-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.

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 2-C methyl erythritol phosphate. 2-C 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.

The isoprenoid pathway produces various metabolites that are essential for diverse cellular functions - cholesterol involved in membrane structure, dolichol involved in protein glycosylation, ubiquinone which participates in mitochondrial electron transport and is a membrane antioxidant and digoxin, an inhibitor of Na^+-K^+ ATPase produced by the hypothalamus. Deficiency of ubiquinone has been documented in Parkinson's disease, epilepsy, schizophrenia and multiple sclerosis. Increased levels of EDLA (endogenous digoxin like activity) have been reported in epilepsy, bipolar mood disorder, vasculitis and syndrome X. Altered levels of dolichol have been observed in Alzheimer's disease.

The coexistence of four pathophysiological phenomena - oncogene activation and malignant transformation, neuronal degeneration, psychiatric manifestation and immune activation has been described in motor neuron disease, systemic malignancy, multiple sclerosis and schizophrenia. Autoantibodies have been demonstrated in multiple sclerosis, motor neuron disease, Alzheimer's disease, Down's syndrome, paraneoplastic syndromes and acquired immunodeficiency syndrome. Psychosis has been documented in multiple sclerosis, Alzheimer's disease, Parkinson's disease, neoplasms and AIDS dementia. Lymphoma has been shown to coexist with multiple sclerosis, motor neuron disease, vasculitis and the acquired immunodeficiency syndrome. Viral persistence as an etiological factor has been documented in multiple sclerosis, Parkinson's disease, neoplasms and schizophrenia. Insulin resistance has been reported in Alzheimer's disease. Immune mediated neuropathies and neoplasms are described in syndrome X. This interrelationship between these disorders suggests the possibility that a central dysfunction may exist which could play a

part in the pathophysiology of these disorders. The isoprenoid pathway may be a candidate in this respect in view of many reports on the changes in the concentration of many products of this pathway in many neurological and psychiatric disorders and therefore this pathway was assessed in these disorders. The disorders included in the study are multiple sclerosis, schizophrenia, Parkinson's disease, CNS glioma, syndrome X with multiple lacunar state, Down's syndrome and acquired immunodeficiency syndrome. The isoprenoid pathway was assessed by plasma HMG CoA reductase activity, serum digoxin, ubiquinone and dolichol levels. Digoxin induced membrane Na^{+}-K^{+} ATPase can produce magnesium depletion and therefore serum magnesium was assessed in all these disorders. Digoxin, apart from affecting cation transport is also reported to influence the transport of various metabolites across cellular membranes, including amino acids and various neurotransmitters. Two of the amino acids in this respect are important, tryptophan, a precursor for strychnine and nicotine and tyrosine a precursor for morphine. Ongoing studies in our laboratory have shown the presence of endogenous morphine in the brain of rats loaded with tyrosine and endogenous strychnine and nicotine in the brain of rats loaded with tryptophan. In view of these the level of the following substances was assessed in the serum of the patients of the disorders studied - concentration of tryptophan and its metabolites (serotonin, quinolic acid, strychnine and nicotine) and the concentration of tyrosine and its metabolites (dopamine, norepinephrine and morphine). The Mg^{++} depletion produced by digoxin and membrane Na^{+}-K^{+} ATPase inhibition can affect the metabolism of glycosaminoglycans, glycoproteins and glycolipids. The elevation in the level of dolichol may suggest its increased availability of N-glycosylation of proteins. The concentration of glycosaminoglycans, carbohydrate components of glycoprotein, glycolipids and glycohydrolases was studied in the serum in all these disorders. Alteration in ubiquinone levels and altered intracellular

calcium/magnesium ratios can affect free radical metabolism. The free radical metabolism was studied in all these orders. The isoprenoid metabolites ubiquinone, dolichol and digoxin can affect membrane structure and function. Therefore RBC membrane composition was studied in all these disorders. A family with coexistence of schizophrenia, Parkinson's disease, neoplasms, rheumatoid arthritis, syndrome X and increased incidence of left handedness with hyperdigoxinemia has been described previously. The isoprenoid pathway related biochemical cascade was also assessed in the family members. The isoprenoid pathway was also assessed in left handed and right handed individuals to find out whether cerebral dominance can affect the operation of the isoprenoid pathway. The results are presented in this paper as well as a hypothesis discussing the central role of hypothalamic archaeal digoxin in conscious perception, neuro-immuno-endocrine integration and coordination of cellular functions. The relationship between digoxin status and cerebral dominance is also discussed. The role of these factors in the pathogenesis of these disorders is also highlighted.

Results

(1) The results showed that HMG CoA reductase activity serum digoxin and dolichol were increased in all these disorders and in the family described indicating upregulation of the isoprenoid pathway but serum ubiquinone was reduced in all these disorders and in the indexed family.

(2) The results showed that the concentration of tryptophan, quinolinic acid and serotonin was found to be higher in the plasma of patients with all these disorders and in the family described while that of tyrosine, dopamine and norepinephrine was lower. Serum of patients with multiple sclerosis showed the presence of morphine. Serum of patients with epilepsy, PD, schizophrenia, multiple sclerosis syndrome X with multiple

lacunar state and the indexed family showed the presence of strychnine. Serum of patients with epilepsy, Parkinson's disease, syndrome X, schizophrenia, CNS glioma patients and the indexed family contained detectable amounts of nicotine.

(3) There was increase in lipid peroxidation as evidenced from the increase in the concentration of MDA, conjugated dienes, hydroperoxides and NO with decreased antioxidant protection as indicated by decrease in ubiquinone and reduced glutathione in most of the disorders and the indexed family studied. The activity of enzymes involved in free radical scavenging like superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase and catalase is decreased in the above disorders and the indexed family studied suggesting reduced free radical scavenging.

(4) The results show an increase in the concentration of serum total GAG, glycolipids (ganglioside, glycosyl-diglyceride, cerebrosides and sulphatides) and carbohydrate components of glycoproteins (hexose, fucose and sialic acid) in all the disorders and in the indexed family studied. The increase in the carbohydrate components'em-total hexose, fucose and sialic acid - in the disorders studied was not to the same extent in all cases suggesting qualitative change in glycoprotein structure. For example in epilepsy, the percentage change in total hexose, fucose and sialic acid when compared to the control is 54.3%, 20% and 33% respectively. The pattern of change in individual GAG in the serum was different, however heparan sulphate (HS) and chondroitin sulphates (ChS) increased in most of the disorders and in the indexed family studied. The activity of GAG degrading enzymes (beta glucuronidase, beta N-acetyl hexosaminidase, hyaluronidase and cathepsin-D) and that of glycohydrolases (beta galactosidase, beta

fucosidase and beta glucosidase) showed significant increase in the serum in most cases and in the indexed family.

(5) The cholesterol: phospholipid ratio of the RBC membrane was increased in glioma, the indexed family and schizophrenia decreased in MS and PD and was not significantly altered in epilepsy. The concentration of total GAG, hexose and fucose of glycoproteiri decreased in the RBC membrane and increased in the serum suggesting their reduced incorporation into the membrane and defective membrane formation in these disorders and in the indexed family.

(6) The left handed individuals as compared to right handed individuals had elevated HMG CoA reductase activity, with increased serum digoxin and dolichol levels. The serum ubiquinone, serum magnesium and RBC Na^{+}-K^{+} ATPase activity were reduced in left handed individuals. The left handed individuals compared to right handed individuals had elevated levels of serum tryptophan, quinolinic acid, serotonin, nicotine and strychnine in the serum. The levels, of tyrosine, dopamine, noradrenaline and morphine were lower in the left handed individuals.

(7) The pattern of incidence of diseases and behavioural patterns in the indexed family showed a high prevalence of Parkinson's disease (8%), schizophrenia (23%), neoplasms (20%), syndrome X (33%), rheumatoid arthritis (16%) and epilepsy (6.6%). The psychological behavioural patterns of the family were as follows - creativity and high IQ (60%), hypersexual behaviour (60%), reduced appetite and eating behaviour (60%), insomnia and reduced sleep patterns (60%), increased tendency for spirituality (80%), increased tendency for addiction (50%) and less of bonding and affectionate behaviour (75%). 30% of the family members were left handed.

Discussion

Archaeal Digoxin and Membrane Na^+-K^+ ATPase Inhibition

The increase in endogenous digoxin, a potent inhibitor or membrane Na^+-K^+ ATPase, can decrease this enzyme activity. In all the disorders studied there was significant inhibition of the RBC membrane Na^+-K^+ ATPase and this inhibition appears to be a common feature for neuropsychiatric disorders. The inhibition of Na^+-K^+ ATPase by digoxin is known to cause an increase in intracellular calcium resulting from increased Na^+-Ca^{++} exchange, increased entry of Ca^{++} via the voltage gated Calcium channel and increased release of Ca^{++} from intracellular endoplasmic reticulum Ca^{++} stores. This increase in intracellular Ca^{++} by displacing Mg^{++} from its binding sites causes a decrease in the functional availability of Mg^{++}. This decrease in the availability of Mg^{++} can cause decreased mitochondrial ATP formation which along with low Mg^{++} can cause further inhibition of Na^+-K^+ ATPase, since the ATP-Mg^{++} 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 Mg^{++} related mitochondrial dysfunction results in defective calcium extrusion from the cell. There is thus a progressive inhibition of Na^+-K^+ ATPase activity first triggered by digoxin. Low intracellular Mg^{++} and high intracellular Ca^{++} consequent to Na^+-K^+ ATPase inhibition appear to be crucial to the pathophysiology of these disorders. The intracellular positive Ca^{++} signal and negative Mg^{++} signal can regulate a diverse cellular process. Ca^{++} on entry into the cell is used to charge up the internal endoplasmic reticulum stores which then release a burst of signal calcium responsible for activating a large variety of calcium dependent cellular processes. The information processing capability of the calcium signalling system is enhanced by amplitude and frequency

modulation. The Ca^{++} is released from channels on internal ER individually or in small groups (blip/quark and puffs/sparks). Further diversity of calcium signalling is produced by compartmentalization as the cytosolic calcium signal and nuclear calcium signal. Serum Mg^{++} was assessed in all these disorders and was found to be reduced. Increased intracellular calcium can lead on to basal ganglia calcification noticed in the family members.

Archaeal Digoxin and Regulation of Neurotransmitter Synthesis and Function

There is an increase in tryptophan and its catabolites and a reduction in tyrosine and its catabolites in the serum of patients with all these disorders. This could be due to the fact that digoxin can regulate the neutral amino acid transport system with preferential promotion of tryptophan transport over tyrosine. The decrease in membrane Na^{+}-K^{+} ATPase activity in all the disorders studied could be due to the fact that the hyperpolarising neurotransmitters (dopamine, morphine and noradrenaline) are reduced and the depolarising neuroactive compounds (serotonin, strychnine, nicotine and quinolinic acid) are increased.

The schizoid neurotransmitter pattern of reduced dopamine, noradrenaline and morphine and increased serotonin, strychnine and nicotine is common to all the disorders studied and could predispose to their development. Quinolinic acid, an NMDA agonist can contribute to the NMDA excitotoxicity reported in schizophrenia. Strychnine by blocking glycinergic transmission can contribute to the decreased inhibitory transmission in schizophrenia. Recent data suggest that the initial abnormality in schizophrenia involves a hypodopaminergic state and the low dopamine levels now observed agrees with this. Nicotine by interacting with nicotine receptors can facilitate the release of dopamine, promoting the dopaminergic transmission in the brain. This can explain the increased dopaminergic transmission in the presence of decreased dopamine

levels. The increase in serotoninergic activity and reduced noradrenergic outflow from the locus coeruleus reported earlier in schizophrenia agrees with our finding of elevated serotonin and reduced noradrenaline levels.

In the presence of hypomagnesmia, the Mg^{++} block on the NMDA receptor is removed leading to NMDA exeitotoxicty. The increased presynaptic neuronal Ca^{++} can produce cyclic AMP dependent phosphorylation of synapsins resulting in increased neurotransmitter release into the synaptic junction and vesicular recycling. Increased intracellular Ca^{++} in the post synaptic neuron can also activate the Ca^{++} dependent NMDA signal transduction. The plasma membrane neurotransmitter transporter (On the surface of the glial cell and presynaptic neuron) is coupled to a Na^{+} gradient which is disrupted by the inhibition of Na^{+}-K^{+} ATPase. resulting in decreased clearance of glutamate by presynaptic and glial uptake at the end of synaptic transmission. By these mechanisms, inhibition Na^{+}-K^{+} ATPase can promote glutamatergic transmission. The elevated levels of quinolinic acid, strychnine and serotonin can also contribute to NMDA excitotoxicity. Strychnine displaces glycine from its binding sites and inhibits glycinergic inhibitory transmission in the brain. The glycine is free to bind to the strychnine insensitive site of the NMDA receptor and promote excitatory NMDA transmission. Quinolinic acid and serotonin are also positive modulators of the NMDA receptor. Increased glutamatergic transmission resulting in excitotoxicity has been implicated in neuronal degeneration observed in Parkinson's disease, primary generalised epilepsy, schizophrenia and AIDS dementia. Inhibition of Na^{+}-K^{+} ATPase can also result in defective neuronal membrane repolarisation and a paroxysmal depolarization shift resulting in epileptogenesis.

Thus in the right hemisphere dominant hyperdigoxinemic state there is upregulated serotoninergic, cholinergic and glutamatergic transmission and downregulated dopaminergic, glycinergic and noradrenergic transmission.

Endosymbiotic Archaeal Induced Hyperdigoxinemic State and Hemispheric Dominance

In left handed individuals there was a derangement of the isoprenoid pathway. They had upregulated HMG CoA reductase activity with increased digoxin and dolichol levels and reduced ubiquinone levels. The RBC membrane Na^+-K^+ ATPase activity was reduced and serum magnesium depleted. The isoprenoid pathway metabolites - digoxin, dolichol and ubiquinone, membrane Na^+-K^+ ATPase and serum magnesium levels were normal in right handed individuals. The left handed individuals had increased levels of tryptophan, serotonin, quinolinic acid, strychnine and nicotine while the levels of tyrosine, dopamine, noradrenaline and morphine were lower. Thus an upregulated isoprenoid pathway, increased level of tryptophan and its catabolites and hyperdigoxinemia is suggestive of right hemispheric dominance. Altered right hemispheric function has been described in several of these disorders. In infantile schizophrenia or autism right hemispheric dysfunction is noticed. In the Lewy body variant of Parkinson's disease right hemispheric dysfunction is documented. In immune mediated disorders also increased left handedness and right hemispheric dominance has been described. Epileptic individuals have a heightened sense of creativity and dominant right hemispheric function. The disorders described - schizophrenia, neoplasms, degeneration, epilepsy, multiple sclerosis, acquired immunodeficiency syndrome and syndrome X may have right hemispheric chemical dominance contributing to their pathogenesis. The hyperdigoxinemic state is seen in normal left handed individuals and may indicate right hemisphermic dominance. We had earlier reported a family with

hyperdigoxinemia and coexistence of schizophrenia, epilepsy, Parkinson's disease, rheumatoid arthritis, syndrome X, neoplasms and left handedness. The analysis of the members of the family also showed the following behavioural pattern. There was an increased tendency for spirituality in 75% of the family members. Temporal lobe epileptic phenomenon has been described in spiritual individuals. There was an increase in creativity and intelligence and the family members had a very high IQ. Increased glutamatergic transmission is associated with memory and intelligence. They had a tendency towards reduced appetite and eating behaviour. Increased serotoninergic transmission can lead on to reduced appetite. There was also hypersexual behaviour in the majority of the family members. This could be related to increased production of nitric oxide in hyperdigoxinemic individuals. Nitric oxide has been related to erectile function. There was an increased tendency to addictive behaviour in family members. Endogenous morphine deficiency has been related to addiction. Morphine synthesis is low in members of the indexed family because of low lyrosine levels. There was a tendency of insomnia and reduced sleep. This could be related to reduced levels of morphine. There was less of bonding and affectionate behaviour. Bonding and affectionate behaviour has been related to doparnine. Dopamine deficiency in hyperdigoxinemic individuals could contribute to less bonding and affectionate behaviour.

Endosymbiotic Archaeal Digoxin and Conscious Perception

The increase in serum digoxin levels in schizophrenia is significant. It has been postulated that there is an underlying generalised disorder of consciousness or self awareness that impairs the ability of think with meta-representations in schizophrenia. Digoxin, a membrane Na^+-K^+ ATPase inhibitor may probably regulate conscious perception. The elements of conscious perception include perceptual binding, focussed attention and short

term memory. The evidence of increased hypothalamic archaeal digoxin points to the role for the hypothalamus. The hypothalamus is connected to the thalamus by the mamillothalamic tract and digoxin may play a role in regulating these synapses. There are two way connections between the cerebral cortex and the thalamic nucleus. There are also two way Connections between the cerebral cortex and hypothalamus and digoxin may possibly regulate these synapses also. The hypothalamus-thalamus-cerebral cortex circuit would play a role in mediating conscious perception. Perceptual binding important in consciousness occurs when all the neurons associated with any one object's perceptual map in layer 5 of the cerebral cortex fire in bursts and in a synchronised pattern but out of synchrony with those representing other objects. When an object is perceived there is a simultaneous activation of the cerebral cortex-hypothalamic two-way connections and liberation of digoxin from the hypothalamus to stimulate the widely dispersed cerebral cortical neurons receiving the incoming perception and their resultant synchronised burst firing. Digoxin by the sodium potassium ATPase inhibition it produces can lead on to a paroxysmal depolarisation shift resulting in sustained synchronised burst firing of cerebral cortical neurons. Short term memory important in conscious perception depends on the hypothalamic-thalamic-cerebral cortex reverberatory circuit as well as the phenomena of sustained synchronised burst firing of neurons in layer 5 of the cerebral cortex. Sustained synchronised burst firing produced by digoxin can temporarily strengthen the relevant synapses so that this particular pattern of firing is recalled quickly - a type of short term memory. Transient synaptic changes of this type are due to alteration in the presynaptic neuronal calcium produced by digoxin. The thalamic-cerebral cortex reverberatory circuit mediating short term memory is glutamatergic and digoxin could amplify the circuit by its inhibitory effect on glial uptake of glutamate and by increasing the synaptic glutamate content.

All axons that pass either way between the cerebral cortex and thalamic nuclei must go through the thalamic reticular nucleus and all give off collateral excitatory glutamatergic branches that innervate the reticular nucleus. The reticular nucleus in turn provides an inhibitory GABAergic innervation back to the thalamic nucleus that provides the input. The reticular nucleus is involved in mediating selective attention by intensifying or detaching a particular active thalamic input into the cortex. The amplification (or focussing) and detachment of attention occurs due to digoxin's effect in promoting glutamatergic transmission in the collaterals to the reticular nucleus by inhibiting the glial uptake of the glutamate and increasing its synaptic content. The back projections from the cerebral cortical perceptual map of the external world to the hypothalamus decides whether hypothalamic archaeal digoxin should act on the glutamatergic collaterals to reticular nucleus and thus focus or detach attention. In schizophrenia, hypersensitivity to perceptual stimulae is noticed as a deficit and patients find it difficult to screen out various stimuli and to focus on one piece of information. The defective stimulus barrier causes difficulty throughout every phase of development. The increased secretion of digoxin produces a hyperconscious state with increased focussed attention, perceptual binding and short term memory. The altered glycoconjugates in schizophrenia lead to disordered synaptic connectivity in the hypothalamo-thalamo-cerebral cortical circuit leading to disordered conscious perception. Cortical cytoarchitectural disorganization of the temporolimbic cortex has been reported in schizophrenia. Elevated levels of serum digoxin and schizoid neurochemical pathology are common to all the disorders studied and could predispose to their development (In the hyperdigoxinemic right hemisphere over dominant state conscious perceptive mechanism are disrupted leading on to a schizoid state).

Endosymbiotic Archaeal Digoxin and Regulation of Golgi Body / Lysosomal Function

The elevation in the level of dolichol may suggest its increased availability of N-glycosylation of proteins. Magnesium deficiency can lead on to defective metabolism of sphinganine producing its accumulation which may lead to increased cerebroside and ganglioside synthesis. In Mg^{++} deficiency the glycolysis, citric acid cycle and oxidative phosphorylation are blocked and more glucose 6-phosphate is channelled for the synthesis of glycosaminoglycans (GAG). Intracellular Mg^{++} deficiency also results in defective ubiquitin dependent proteolytic processing of glycoconjugates as it requires Mg^{++} for its function. The increase in the activity of glycohydrolases and GAG degrading enzymes could be due to reduced lysosomal stability and consequent leakage of lysosomal enzymes into the serum. The increase in the concentration of carbohydrate components of glycoproteins and GAG in spite of increased activity of many glycohydrolases may be due to their possible resistance to cleavage by glycohydrolases consequent to qualitative change in their structure. Proteoglycan complexes formed in the presence of altered Ca^{++}/Mg^{++} ratios intracellularly may be structurally abnormal and resistant to lysosomal enzymes and may accumulate.

Previous reports of alteration in glycoproteins in this connection include alteration in alpha acid glycoprotein (AAG) and beta amyloid precursor protein in epilepsy and Alzheimer's disease and alpha synuclein in Parkinson's disease. Structurally abnormal glycoproteins resist catabolism by lysosomal enzymes and accumulate in neuronal degeneration. Interaction between HS-proteoglycan and ChS-proteoglycan with proteins like beta amyloid, tau protein, parkin and alpha synuclein and reduced proteolytic digestion of these complexes leading on to their accumulation in the neurons have been reported in neurodegenerative diseases like Alzheimer's disease and Parkinson's disease. Alteration in the

sulphated proteoglycan matrix of the synaptic vesicles can alter neurotransmitter release into the synapse and produce a functional disorder like schizophrenia and epilepsy. Membrane Na^{+}-K^{+} ATPase inhibition can lead to defective notch signalling. Notch is a transmembrane protein that acts as a signal receptor and is important in neurogenesis. Neuronal growth by extending neurites and forming connections is regulated by the notch signalling pathway. The notch signalling inhibits extension of neurites and keeps them stable in the mature brain. A notch ligand known as delta regulates neurogenesis by binding to notch in membranes of embryonal cells and prevents them from developing along the neuronal pathway. Notch activation by the ligand causes notch to be cleaved releasing the notch intracellular domain. This then passes into the nucleus and activates transcription as part of the DNA binding complex with CSL protein. Intracellular cleavage of the notch is regulated by presenilin and also depends upon the lysosomal protease. In the presence of a lysosomal instability consequent to defective lysosomal membranes notch cleavage by protease is defective leading on to functional disorders consequent to defective synaptic connectivity. The defective notch signalling pathway can lead on to neuronal degeneration. Altered glycoproteins, glycolipids and GAG of the neuronal membrane can also contribute to schizophrenia and epilepsy by producing disordered synaptic connectivity.

The protein processing defect can result in defective glycosylation of endogenous myelln glycoprotein antigens and exogenous viral glycoproteins antigens with consequent defective formation of the MHC-antigen complex. The MHC linked peptide transporter, a Pglycoprotein which transports the MHC-antigen complex to the antigen presenting cell surface has an ATP binding site. The peptide transporter is dysfunctional in the presence of Mg^{++} deficiency. This results in defective transport of the MHC class-1 glycoprotein antigen complex to the antigen presenting cell surface for recognition by the

CD_4 or CD_8 cell. Defective presentation of the endogenous myelin glycoprotein antigen can explain the immune dysregulation in MS. A CD_8 MHC class-1 restricted immune dysregulatory defect has been described in MS. Defective presentation of exogenous viral antigens can produce immune evasion by the virus as in AIDS dementia. Viral persistence has been implicated in the development of tumours (ebstein barr virus and lymphoma), degenerations (Parkinson's disease and corona virus) and schizophrenia (borna virus disease). A number of fucose and sialic acids containing natural ligands are involved in trafficking of leukocytes and similar breaches in the blood brain barrier and adhesion of the lymphocyte producing leukocyte trafficking and extravasation in to the perivascular space have been described in MS. Altered myelin glycoprotein due to defective glycosylation and alteration in GAG of proteoglycans of myelin can affect the structural integrity of myelin leading on to demyelination. Abnormally glycosylated tumour antigens can lead to defective tumour antigen presentation and loss of immunosurveillance by the natural killer cells. Altered cell surface glycoproteins, glycolipids and GAG can lead to defective contact inhibition and oncogenesis. A number of fucose and sialic acids containing natural ligands have been implicated in neoplastic transformation and metastasis. The MHC glycoproteins are involved in formation of synaptic connectivity during neuronal development. Defective formation and presentation of the MHC - neuronal glycoprotein complex can lead on to disordered synaptic connectivity and functional disorders like schizophrenia and epilepsy.

Thus in the hyperdigoxinemic right hemisphere dominant state there is reduced lysosomal stability, defective ubiquitin dependent proteolytic processing of proteins and alteration in the glycoconjugate structure leading on to their defective catabolism and accumulation. There is also a defect in the MHC antigen presenting pathway leading on to immunodysregulation and viral persistence.

Endosymbiotic Archaeal Digoxin and Alteration in Membrane Structure and Membrane Formation

The alteration in the isoprenoid pathway specifically, cholesterol as well as changes in glycoproteins and GAG can affect cellular membranes. The upregulation of isoprenoid pathway can lead to increased cholesterol synthesis and Mg^{++} deficiency can inhibit phospholipid synthesis. Phospholipid degradation is increased owing to increase in intracellular calcium activating phospholipase A_2 and D. The cholesterol: phospholipid ratio of the RBC membrane was increased in glioma, the indexed family and schizophrenia, decreased in MS and PD and was not significantly altered in epilepsy. The concentration of total GAG, hexose and fucose of glycoprotein decreased in the RBC membrane and increased in the serum suggesting their reduced incorporation into the membrane and defective membrane formation. The glycoproteins, GAG and glycolipids of the cellular membrane are formed in the endoplasmic reticulum, which is then budded of as a vesicle which fuses with the golgi complex. The glycoconjugates are then transported via the golgi channel and the golgi vesicle fuses with the cell membrane. This trafficking depends upon GTPases and lipid kinases which are crucially dependent on magnesium and are defective in Mg^{++} deficiency. The change in membrane structure produced by alteration in glycoconjugates and the cholesterol phospholipid ratio can produce changes in the conformation of Na^{+}-K^{+} ATPase resulting in further membrane Na^{+}-K^{+} ATPase inhibition. The same changes can affect the structure of the organelle membrane. This results in defective lysosomal stability and leakage of glycohydrolases and GAG degrading enzymes into the serum. Defective peroxisomal membranes lead to catalase dysfunction which has been documented in these disorders. Thus in the hyperdigoxinemic right hemisphere dominant state there is defective membrane formation, membrane structure and function.

Endosymbiotic Archaeal Digoxin and Mitochondrial Dysfunction

The concentration of ubiquinone decreased significantly in most of the cases which may be the result of low tyrosine levels, reported in most of the disorders, consequent to digoxin's effect in preferentially promoting tryptophan transport over tyrosine. The aromatic ring portion of ubiquinone is derived from tyrosine. Ubiquinone, which is an important component of the mitochondrial electron transport chain, is a membrane antioxidant and coniributes to free radical scavenging. The increase in intracellular Ca^{++} can open the mitoehondrial PT pore causing a collapse of the H^{+} gradient across the inner membrane and uncoupling of the respiratory chain. Intracellular Mg^{++} deficiency can lead to a defect in the function of ATP synthase. All this leads to defects in mitochondrial oxidative phosphorylation, incomplete reduction of oxygen and generation of the superoxide ion which produces lipid peroxidation. Ubiquinone deficiency also leads to reduced free radical scavenging. The increase in intracellular calcium may lead to increased generation of NO by inducing the enzyme nitric oxide synthase which combines with the superoxide radical to form peroxynitrite. Increased calcium also can activate phospholipase A_2 resulting in increased generation of arachidonic acid which can undergo increased lipid peroxidation. Increased generation of free radicals like the superoxide ion, and hydroxyl radical can produce lipid peroxidation and cell membrane damage which can further inactivate Na^{+}-K^{+} ATPase, triggering the cycle of free radical generation once again. Mg^{++} deficiency can affect glutathione synthetase and glutathione reductase function. The mitochondrial superoxide dismutase leaks out and becomes dysfunctional with calcium related opening of the mitochondrial PT pore and outer membrane rupture. The peroxisomal membrane is defective owing to the membrane Na^{+}-K^{+} ATPase inhibition related defect in membrane formation and leads to reduced catalase activity. Mitochondrial dysfunction related free radical generation has been

implicated in the pathogenesis of neuronal degeneration oncogenesis and immune mediated disorders.

The increased intracellular calcium and ceramide related opening of the mitochondrial PT pore also leads to volume dysregulation of the mitochondria causing hyperosmolality of the matrix and expansion of the matrix space. The outer membrane of the mitochondria ruptures and releases apoptosis inducing factor and cytochrome C into the cytoplasm. This results in activation of caspase-9 and caspase-3. Caspase-9 can produce apoptosis of the cell. Apoptosis has been implicated in neuronal degeneration. Apoptosis can produce defective synaptogenesis and synaptic connectivity contributing to functional disorders like schizophrenia and epilepsy. Apoptosis of the CD_4 cell can contribute to CD_4 depletion in the acquired iinmunodeficiency syndrome. Oligodendrocyte (the myelin forming cell) apoptosis is crucial to the pathogenesis of MS. Caspase-3 activation can cleave P_{21} involved in linking DNA duplication to cell division resulting in a polyploid cell and oncogenesis. We have been able to demonstrate neuronal degneration and apoptosis in the digoxin injected rat brain.

Thus in the hyperdigoxinemic right hemisphere dominant state there is a defect in mitochondrial function and increased free radical generation and reduced scavenging. There is also increased apoptosis.

Endosymbiotic Archaeal Digoxin and Immunoregulation

Increased intracellular calcium activates the calcium dependent calcineurin signal transduction pathway which can produce T-cell activation and secretion of interleukin - 3, 4, 5, 6 and TNF alpha (Tumour necrosis factor alpha). TNF alpha binds to its receptor TNFRI and activates the transcription factors HFkB and AP-1 leading to the induction of proinflammatory and immunomodulatory

genes. This can also explain the immune activation in MS. TNF alpha can also bring about apoptosis of the cell. It binds to its receptor and activates caspase-9, an ICE protease which converts IL-1 beta precursor to IL-1 beta. IL-1 beta produces apoptosis of the neurons (in Alzheimer's disease and AIDS dementia), oligodendrocyte-the myelin forming cell in MS and the CD_4 cell in HIV infection. IL-1 beta and TNF alpha induce HIV protein expression by the transcription related mechanism and contributes to the pathogenesis of AIDS dementia. Membrane Na^+-K^+ ATPase inhibition can produce immune activation and is reported to increase CD_4/CD_8 ratios as exemplified by the action of lithium. The hyperdigoxinemic right hemisphere dominant State results in immune activation.

Endosymbiotic Archaeal Digoxin and Regulation of Cell Division, Cell Proliferation and Neoplastic Transformation

Intracellular magnesium depletion can produce defective phosphorylation of MAP (microtubule associated proteins). This results in defective microtubule related spindle fibre dysfunction and chromosomal non-dysjunction probably contributing to trisomy 21.

Increased intracellular calcium activates phospholipase C beta which results in increased production of diacyglycerol (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. Upregulation of isoprenoid pathway can result in increased production of

farnesyl phosphate which can farnesylate the ras oncogene producing its activation. The ubiquitin system of catabolic processing of processing of proteins is important in the DNA repair mechanism. In the presence of intracellular magnesium deficiency ubiquitin protein catabolic processing and DNA repair mechanisms are defective and this could contribute to oncogenesis. In the hyperdigoxinemic right hemisphere dominant State there is oncogene activation and increased cell proliferation.

Endosymbiotic Archaeal Digoxin and the Metabolic Regulation

Inhibition of Na^+-K^+ ATPase can also explain the pathogenesis of syndrome X. Increased TNF alpha as mentioned above consequent to Na^+-K^+ ATPase inhibition related T-cell activation can contribute to insulin resistance in syndrome X at the receptor level. Decrease in intracellular magnesium can block the phosphorylation reactions involved in protein tyrosine kinase receptor activity leading to insulin resistance. Increase in beta cell calcium can contribute to increased insulin release from beta cells and hyperinsulinemia. Increased intracellular calcium can activate the G-protein coupled signal transduction of the contra insulin hormones (growth hormone and glucagon) leading to hyperglycemia. Decrease in intracellular magnesium can lead on to inhibition of glycolysis. Decreased intracellular magnesium can lead on to a mitochondrial ATP synthase defect. Increased intracellular calcium can open up the mitochondrial PT pore, disrupt the H^+ gradient across the inner membrane and block mitochondrial oxidative phosphorylation. All this leads to defective glucose utilisation and hyperglycemia. Increase in intracellular calcium can activate the Gprotein coupled angiotensin receptor producing hypertension and the G-protein coupled thrombin receptor and platelet activating factor producing thrombosis observed in syndrome X. Na^+-K^+ ATPase inhibition related increased smooth muscle calcium and decreased magnesium can contribute to

vasospasm and ischaemia observed in stroke and CAD. Na^+-K^+ ATPase inhibition related altered glycoprotein can contribute to the microangiopathy and macroangiopathy observed in syndrome X. Metabolic syndrome X could be visualised as being due to hypothalamic archaeal digoxin hypersecretion. In the hyperdigoxinemic right hemisphere dominant state glucose metabolism and utilisation is impaired consequent to insulin resistance as also a tendency for vasospasm and thrombosis.

Endosymbiotic Archaeal Digoxin and Regulation of the Immune Response to Viral Infection

The same biochemical Na^+-K^+ ATPase related cascade described above could contribute to the acquired immunodeficiency syndrome. There is increased incidence of neoplasms like non-Hodgkin's lymphomas and vasculitis in the acquired immunodeficiency syndrome. Neuronal degenerations like AIDS dementia have been related to glutamate excitotoxicity. An AIDS related schizophreniform psychosis has been described. Polyclonal B-cell proliferation and lymphadenopathy have been described in AIDS. Digoxin induced calcineurin signal transduction mediated T-cell activation and polyclonal B-cell proliferation can contribute to HIV-1 replication. This is because chief among the inducible cellular proteins that promote the growth of HIV-l is transcription factor NFkB. HIV-l has incorporated two such NFkB binding-enhancer elements into its own genome, which allows the triggering of HIV-1 transcription in the presence of nuclear NFkB. Digoxin induced protein glycosylation defects can also lead to defective glycosylation of HIV glycoprotein antigens leading on to defective formation of HIV glycoprotein antigen - MHC complex for presentation to the CD_4 cell. This results in immune evasion by the virus and could also contribute to the persistence of the herpes virus and Epstein Barr virus producing Kaposi's sarcoma and non-Hodgkin's

lymphoma respectively. Hypothalamic structural abnormalities have been described in homosexuals predisposed to the development of acquired immunodeficiency syndrome. In the hyperdigoxinemic right hemisphere dominant state there is a tendency for viral persistence consequent to defective processing of viral proteins and defective immune response to the virus.

Endosymbiotic Archaeal Digoxin and Neuro-immuno-endocrine Integration

Hypothalamic archaeal digoxin can thus integrate multiple brain functions. Digoxin can regulate neuronal transmission and conscious perception in the brain by its effect on neutral amino acid and neurotransmitter transport. Digoxin can also play a role in endocrine integration. The hypothalamic hormone secretion is regulated by biogenic amines noradrenaline, dopamine and serotonin. Digoxin, by regulating the release and uptake of these neurotransmitters, can control hypothalamic hormone secretion. Digoxin, by its lithium like action in modulating G-protein function and by facilitating calcium induced signal transduction by increasing Na^{+}-Ca^{++} exchange, can regulate the function of these hormones. Digoxin can act as an immuno-modulator owing to its effect on calcineurin signal transduction in the lymphocyte and subsequent immune activation.

Endosymbiotic Archaeal Digoxin and Integration of Cellular Function

Digoxin can regulate multiple cellular functions. Digoxin can regulate plasma membrane transport as well as membrane structure and fluidity. It can also regulate the fluidity of organelle membranes. Digoxin by its effects of calcium mediated opening of the mitochondrial PT pore and ubiquinone synthesis can regulate mitochondrial function. The dolichol pathway can regulate protein

glycosylation and golgi body function. Digoxin induced hypomagnesemia can regulate the ubiquitin dependent protein catabolic pathway. Digoxin induced change in intracellular magnesium can regulate nuclear function as DNA polymerase, DNA ligase and ribosomes require magnesium for their function. Digoxin by producing magnesium depletion can regulate GAG metabolism and the structure of the cell matrix. Digoxin can regulate cell death or apoptosis by opening up the mitochondrial PT pore consequent to a rise in intracellular calcium it produces. Digoxin by its effect upon ras oncogene can modulate cell proliferation. Digoxin induced hypomagnesemia by producing changes in cell surface glycoproteins and GAG can regulate contact inhibition and cell proliferation. Digoxin can regulate the function of heat-shock protein which coordinates the trafficking and regulation of diverse signalling proteins, and which also functions as a molecular chaperone involved in protein folding and maturation. The heat-shock protein has an ATP/ADP switch domain that regulates hsp conformation and digoxin induced hypomagnesemia can modulate its function. Intracellular magnesium deficiency can regulate phosphorylation of MAP (microtubule associated proteins) and regulate cytoskeletal structure/function.

Digoxin can thus produce conscious perception, neuro-immuno-endocrine integration and integrate the function of multiple cellular organelles. The hyper digoxinemic state is a right hemisphere dominant state.

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Chapter 3

The Hypodigoxinemic Left Hemispheric Dominant Family - Digoxin Deficiency Syndrome - The Homo Sapien Family

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 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. The archaeal symbiosis leads to the evolution of a new human neoneanderthal species. This can be called as the neoneanderthal age or Kali yuga.

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.

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 2-C methyl erythritol phosphate. 2-C methyl erythritol phosphate can be synthesized from erythrose 4-phosphate a metabolite of the shikimic acid pathway. DXP combines with MEP to form isopentenyl pyrophosphate which is converted to cholesterol. Cholesterol is catabolized by archaeal cholesterol oxidases to generate digoxin. The digoxin sugars digitoxose and rhamnose are synthesized by the upregulated pentose phosphate pathway. Glycolytic suppression leads to upregulation of the pentose phosphate pathway. The expressed archaeaon organelle concerned with cholesterol catabolism and digoxin synthesis is called the steroidelle. The suppression of glycolysis and stimulation of fructolysis results in upregulation of the hexosamine pathway. Fructose is converted to fructose 6-phosphate by ketohexokinases. The fructose 6-phosphate is converted to glucosamine 6-phosphate by the action of glutamine fructose 6-phosphate amidotransferase

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

archaeaon particles concerned with the synthesis of vitamin C, vitamin E and ubiquinone which are all antioxidants are called the vitaminocyte.

A family with coexistent hypotension, recurrent respiratory infection owing to immune deficiency, motor tics, obsessive compulsive disorder, major depressive disorder, early onset osteoporosis, low body mass index, bulimia nervosa and healthy aging is described. The family members had the following behavioural patterns - hyposexual, non-spiritual, non-creative, somnolent tendency, increased bonding and affectionate behaviour and non-addictive tendency. All members in the family were right handed left hemispheric dominant. Alteration in the endogenous membrane Na^+-K^+ ATPase inhibitor, digoxin has been documented in depression as well as in essential hypertension. Digoxin is a steroidal glycoside, synthesized in the human hypothalamus by the isoprenoid pathway and is also reported to modulate neuronal transmission. The other isoprenoidal metabolites of significance are ubiquinone (regulate mitochondrial function), cholesterol (component of cellular membranes) and dolichol (regulate N-glycosylation of proteins). Therefore the isoprenoidal pathway, glycoconjugate metabolism, neurotransmitter patterns, free radical metabolism and membrane composition were studied in the indexed family. Since digoxin can regulate synaptic transmission and possibly hemispheric dominance, the isoprenoid pathway was also compared in right hemispheric and left hemispheric dominance to find out whether hemispheric dominance plays a role in the genesis of the disorder.

Materials and Methods

The indexed family was analysed over three generations for motor tics, OCD, major depressive disorder, bulimia nervosa, recurrent respiratory infections, early onset osteoporosis, hypotension and low body-mass index. OCD, major depressive disorder and bulimia nervosa were diagnosed by the DSM-IV criteria.

Recurrent respiratory infections were diagnosed when there were more than three significant respiratory infections in a month that warranted treatment. Low body mass index was defined as a body-mass index less than 18.5 kg/m^2. The family members were screened for the behavioural patterns mentioned below - (i) the criteria given in the handbook for the 16 PF - the 16 personality factors questionnaire was chosen after modification for defining spirituality, creativity and bonding / affection, and (ii) the criteria for insomnia and somnolence, sexual behaviour, addiction and eating behaviour were chosen from the DSM IV criteria. All the 15 alive affected members of the indexed family were chosen for the study except one family member - A_1 who died. Each patient also had an age and sex matched right handed / left hemispheric dominant control. In addition 15 normal left handed individuals who were right hemisphere dominant and 15 right handed individual who were left hemisphere dominant, between the age group 20 and 30 years chosen by the dichotic listening test were also chosen for comparison of the same parameters.

Results

Clinical Features of the Indexed Family

The description of the indexed family is given in table 1. Motor tics was seen in 22% of the family members, OCD in 56%, major depressive disorder in 44%, hypotension in 72%, osteoporosis in 17%, low body mass index in 50%, recurrent respiratory infection with immunodeficiency in 44% and bulimia nervosa in 17%. The family members had hyposexual behaviour (80%), less tendency for spirituality and creativity (70%), had no insomnia but a tendency towards increased somnolence (60%), no addictive behaviour (80%) and had more bonding and affectionate behaviour (80%). One member of the family survived to 99 years of age and was healthy throughout his life span. There was

total lack of incidence of vascular thrombosis, neuronal degeneration and systemic malignancies as well as healthy longevity (average life span of 85 years) in three generations of the indexed family. All members in the family were right handed left hemispheric dominant.

Table 1. *Description of the indexed family.*

Diseases	Percentage
Motor tics	22.22
OCD	55.55
Depression	44.44
Hypotension	72.22
Low body mass index	50.00
Eating behaviour (bulimia)	16.66
Osteoporosis	16.66
Recurrent respiratory infection	44.44

Biochemical Changes in the Indexed Family

The activity of HMG CoA reductase and the concentration of digoxin and dolichol were decreased in familial and left hemispheric dominant cases. The concentration of serum ubiquinone, the activity of erythrocyte membrane Na^{+}-K^{+} ATPase and serum magnesium were increased. The opposite patterns were obtained in right hemispheric dominance. The concentration of serum tryptophan, quinolinic acid and serotonin was decreased while that of tyrosine, dopamine and noradrenaline was increased in the plasma of familial and left hemispheric dominant cases. Nicotine and strychnine were not detected in the plasma of familial and left hemispheric dominant cases. Morphine was detected in the plasma of familial cases (9.56 μg/dL) and left hemispheric dominance (6.92 μg/dL). The opposite patterns were obtained in right hemispheric dominance. Right hemispheric dominant individuals had no detectable morphine in the serum but had detected amounts of strychnine (9.52 μg/dL) and

nicotine (2.07 µg/dL). The concentration of total glycosaminoglycans (GAG) and individual GAG fractions, carbohydrate components of glycoproteins and glycolipids decreased in the serum of familial cases. The activity of glycosaminoglycan (GAG) degrading enzymes and glycohydrolases was decreased in familial cases when compared to the controls. The concentration of total GAG and hexose and fucose residues of glycoproteins in the RBC membrane increased significantly in familial cases.

The concentration of RBC membrane cholesterol decreased while that of phospholipid increased resulting in decreased cholesterol: phospholipid ratio.

The activity of free radical scavenging enzymes, the concentration of reduced glutathione and ceruloplasmin and iron binding capacity increased significantly while the concentration of lipid peroxidation products and nitric oxide decreased significantly in familial cases.

Discussion

Archaeal Digoxin and Membrane Na^+-K^+ ATPase Inhibition in Relation to Digoxin Deficiency Syndrome

The archaeaon steroidelle DXP pathway and the upregulated pentose phosphate pathway contribute to digoxin synthesis. The decrease in the activity of HMG CoA reductase in familial cases suggests a downregulation of the isoprenoid pathway. There is a marked decrease in plasma digoxin and dolichol and this decrease may be a consequence of decreased channelling of intermediates of the isoprenoid pathway for their biosynthesis. The decrease in endogenous digoxin, a potent inhibitor of membrane Na^+-K^+ ATPase, can increase this enzyme activity. The stimulation of Na^+-K^+ ATPase by digoxin is known to cause a decrease in intracellular calcium and an increase in intracellular

magnesium. Serum magnesium was assessed in familial cases and was found to be increased. Decrease in bone calcium load can lead on to osteoporosis.

Archaeal Digoxin and Regulation of Neurotransmitter Synthesis and Function in Relation to Digoxin Deficiency Syndrome

The archaeaon neurotransminoid shikimic acid pathway contributes to tryptophan and tyrosine synthesis and catabolism generating neurotransmitters and neuroactive alkaloids. The results showed that the concentration of tryptophan, quinolinic acid, serotonin, strychnine and nicotine was found to be lower in the plasma of patients with familial cases while that of tyrosine, dopamine, norepinephrine and morphine was higher. Nicotine and strychnine are synthesized from tryptophan and morphine from tyrosine. Thus there is a decrease in tryptophan and its catabolites and increase in tyrosine and its catabolites in the patient's serum. This could be due to the fact that digoxin can regulate the neutral amino acid transport system with a preferential promotion of tryptophan transport over tyrosine and because digoxin levels are low in familial cases. The increase in membrane Na^+-K^+ ATPase activity in familial cases could be due to the fact that the hyperpolarising neurotransmitters (dopamine, morphine and noradrenaline) are increased and the depolarising neuroactive compounds (serotonin, strychnine, nicotine and quinolinic acid) are decreased. The low level of quinolinic acid, serotonin and strychnine can contribute to reduced excitatory glutamatergic transmission as they are all positive modulators of the NMDA receptor. In the presence of hypermagnesemia, the magnesium block on the NMDA receptor is strengthened leading onto reduced NMDA transmission. Reduced glutamatergic transmission can lead on to healthy aging and protect the brain from neuronal degeneration. The depressive syndrome noted in the family could be due to low serotonin. Decreased serotoninergic transmission has been related to depression. The

presence of OCD syndrome in the family could also be related to serotonin depletion. Serotonin depletion has been related to obsessive psychopathology. The presence of motor tics could be related to increased dopaminergic transmission in the brain. Deficiency of serotonin can lead to increased appetite and eating behaviour with bulimia in the family members.

Archaeal Digoxin and Regulation of Golgi Body / Lysosomal Function in Relation to Digoxin Deficiency Syndrome

The archaeaon glycosaminoglycoid and fructosoid contributes to glycoconjugate synthesis and catabolism by the process of fructolysis. Hypermagnesemia and decreased dolichol (required for N-glycosylation) levels can inhibit GAG, glycolipid and glycoprotein biosynthesis. The activity of GAG degrading enzymes and glycohydrolases decreased in the serum suggesting increased lysosomal stability. Intracellular hypermagnesemia also results in increased ubiquitin dependent proteolytic processing of glycoconjugates as it requires magnesium for its function. Defective lysosomal stability and defective degradation of glycoprotein - GAG complexes as in the case of tau protein / amyloid - HS proteoglycan complexes in Alzheimer's disease can lead on to brain aging. Membrane Na^{+}-K^{+} ATPase stimulation could thus protect against neuronal aging and degeneration. A number of fucose and sialic acids containing natural ligands have been implicated in inflammatory responses and neoplastic transformation. The decrease in fucose and sialic acid noted in these cases could lead on to an immunosuppressive state with recurrent respiratory infection and prevent malignant transformation. Decrease in bone structural glycosaminoglycans could contribute to osteoporosis.

Archaeal Digoxin and Alteration in Membrane Structure and Membrane Formation in Relation to Digoxin Deficiency Syndrome

The archaeaon steroidelle, glycosaminoglycoid and fructosoid contribute to cell membrane formation synthesizing cholesterol by the DXP pathway and glycosaminoglycans by fructolysis. The downregulation of the isoprenoid pathway can lead to decreased cholesterol synthesis and magnesium excess can stimulate phospholipid synthesis leading on to decreased membrane cholesterol: phospholipid ratio. The concentration of total GAG and carbohydrate residues of glycoprotein increased in the RBC membrane and decreased in the serum suggesting their increased incorporation into the membrane. Hypermagnesemia can stimulate the activity of membrane trafficking enzymes - GTPases and lipid kinases. The change in membrane structure produced by alteration in glycoconjugates and the cholesterol: phospholipid ratio can produce changes in the conformation of Na^+-K^+ ATPase resulting in further membrane Na^+-K^+ ATPase stimulation. The same changes can affect the lysosomal membrane increasing its stability.

Archaeal Digoxin and Mitochondrial Dysfunction in Relation to Digoxin Deficiency Syndrome

The archaeaon vitaminocyte contributes to the synthesis of ubiquinone and mitochondrial electron transport chain function. The mitochondrial function related free radical generation is regulated by the archaeaon vitaminocyte synthesized tocopherol and ascorbic acid. The concentration of ubiquinone (free radical scavenger and component of the mitochondrial electron transport chain) increased significantly in familial cases which may be the result of increased tyrosine levels, consequent to digoxin deficiency promoting tyrosine transport over tryptophan. The aromatic ring portion of ubiquinone is derived from tyrosine. The decrease in intracellular calcium can stabilise the mitochondrial

PT pore and improve mitochondrial function. Intracellular hypermagnesemia can lead on to increased ATP synthase activity. All this leads to improved efficiency of mitochondrial oxidative phosphorylation and reduced free radical generation. Decreased intracellular calcium also leads to decreased generation of NO by inhibiting the enzyme nitric oxide synthase and reduced peroxynitrite formation. The free radical scavenging enzyme activity, the concentration of antioxidants (ubiquinone, reduced glutathione, ceruloplasmin) and iron binding capacity increased significantly in familial cases suggesting increased free radical scavenging. The peroxisomal membrane is stabilised owing to membrane Na^{+}-K^{+} ATPase stimulation related upregulation in membrane formation and leads to increased catalase activity. Hypermagnesemia leads to increased glutathione synthetase, glutathione peroxidase and glutathione reductase function. The stabilisation of the mitochondrial PT pore consequent to reduced intracellular calcium produces increased efficiency of superoxide dismutase activity. Mitochondrial dysfunction related free radical generation has been implicated in the pathogenesis of neuronal degeneration like PD, oncogenesis and inflammatory diseases. The reduced generation of free radicals leads to decreased incidence of neuronal degeneration and oncogenesis in the index family. Free radicals are required for lymphocyte activation and this leads to a hypoimmune response and increased respiratory infection owing to immunodeficiency. The decreased intracellular calcium and ceramide related stabilisation of the mitochondrial PT pore inhibits cytochrome C release and the caspase cascade. Apoptosis has been implicated in neuronal degeneration and its inhibition protects against neuronal aging.

Archaeal Digoxin and Regulation of Cell Division, Cell Proliferation and Neoplastic Transformation in Relation to Digoxin Deficiency Syndrome - 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. There is a decreased oncogenic tendency in the indexed family. Decreased intracellular calcium inactivates phospholipase C beta which results in decreased production of diacylglycerol (DAG) with resultant inactivation of protein kinase C and the MAP kinase cascade. The intracellular hypermagnesemia can produce increase in the GTPase activity of the alpha subunit of G-protein resulting in ras oncogene inactivation, as more of the ras is bound to GDP rather than GTP. Tumour suppressor gene, P_{53} activation is increased owing to intracellular hypermagnesemia producing increased phosphorylation. Decreased intracellular calcium inactivates the calcium dependent calcineurin signal transduction pathway involved in T-cell activation and reduces the secretion of interleukin-3,4,5,6 and TNF alpha. TNF alpha can also bring about apoptosis of the cell and this is inhibited. TNF alpha binds to its receptor TNFRI and activates the transcription factors NFkB and AP-1 leading to induction of proinflammatory and immunomodulatory genes. Low levels of TNF alpha can lead to immunosuppression in the family.

Digoxin Deficiency Syndrome and Reverse Metabolic Syndrome X

Hypermagnesemia can upregulate glucose transport as magnesium is required as a cofactor for cell membrane glucose transport. Intracellular hypennagnesemia can activate the phosphorylation reactions involved in protein tyrosine kinase receptor activity leading to increased insulin receptor activity. Intracellular hypermagnesemia can lead on to stimulation of glycolysis.

Decrease in intracellular calcium can stabilise the mitochondrial PT pore and stimulate mitochondrial oxidative phosphorylation. Intracellular hypermagnesemia can also lead to ATP synthase hyperactivity. This leads to increased glucose utilisation. Decrease in beta cell calcium and increase in magnesium can contribute to decreased insulin release from beta cells and hypoinsulinemia. Increased intracellular magnesium can produce hyperactivity of lipoprotein lipase producing increased catabolism of triglycerides rich lipoproteins and hypotriglyceridemia. In hypermagnesemia, Lecithin cholesterol acyl transferase (LCAT) is increased and there is increased formation of cholesterol esters in HDL. This results in increased HDL cholesterol. Magnesium excess has been reported to decrease LDL cholesterol levels also. Low insulin levels and increased triglyceride catabolism can be correlated with low body mass index noted in the family. Decreased in intracellular calcium can inactivate G-protein coupled angiotensin receptor producing hypotension and G-protein coupled thrombin receptor and platelet activating factor producing decreased thrombosis observed in the family. Increased intracellular magnesium can lead to decreased thrombin and ADP / collagen induced platelet aggregation. Na^{+}-K^{+} ATPase stimulation related decreased smooth muscle calcium and increased magnesium can contribute to vasodilatation and protect the family from ischaemia due to stroke and CAD. The family has an endogenous morphine excess syndrome. Morphine has been reported to have an effect on glucose metabolism. Intrathecal administration of morphine in the lumbar region causes a dose-dependent hypoglycemia. Morphine can also regulate insulin release from the beta cells with an inhibitory effect reported in some cases. Morphine has also got an immunosuppressive action. This could contribute to increased incidence of respiratory infections. Morphine excess can lead on to lack of addiction which has been noticed in the family membrane.

Archaeal Digoxin and Hemispheric Dominance in Relation to Digoxin Deficiency Syndrome

The archaeaon related organelle - steroidelle, neurotransminoid and vitaminocyte contribute to hemispheric dominance. The biochemical pattern obtained in the family correlated with the left hemispheric dominant state. In the left hemispheric dominant state there is a downregulated isoprenoid pathway, hypodigoxinemia, membrane Na^+-K^+ ATPase stimulation, decreased dolichol synthesis and elevated ubiquinone synthesis. There is an upregulated morphinergic, dopaminergic and noradrenergic transmission with a downregulated glutamatergic, cholinergic / nicotinic and serotoninergic transmission. There are no previous reports on a hypodigoxinemic syndrome in literature as also studies on biochemical differences between right and left hemispheric dominance.

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GLOBAL WARMING

and Symbiotic Evolution of Species

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Archaea and Viroid Induced Symbiotic Human Evolution and Hemispheric Dominance

Archaea and Viroid Induced Symbiotic Human Evolution - Vitaminocyte Organelle and Brain Evolution

Archaea and Viroid Induced Symbiotic Human Evolution and the Steroidelle - The Isoprenoid Cholesterol Organism

Archaea and Viroid Induced Symbiotic Human Evolution - Retrovirus, Prions and Viroids - Porphyrinoids and Viroidelle

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