

Chapter 4

Global Warming Induced Endosymbiotic
Actinidic Archaeal Synthesis of Digoxin from
Cholesterol Regulates Cellular Function and
Contributes to Disease Pathology

Introduction

Climate change and related stress leads to increased porphyrin synthesis leading onto porphyrinuria and porphyria. The stimulus for porphyrin synthesis comes from heme deficiency. Heme suppresses ALA synthase. Stress induces heme oxygenase which converts heme to carbon monoxide and bilirubin. Thus heme is depleted from the system. Heme oxygenase is induced by environmental stress. Climatic changes of global warming and ice age can induce heme oxygenase. Heme oxygenase is also induced by EMF pollution of the environment. Thus there is increased porphyrin synthesis from succinyl CoA and glycine. The porphyrins can self organize to form macromolecular structures which can self replicate to form a porphyrin organism.¹ The photon induced transfer of electrons along the macromolecule can lead to light induced ATP synthesis. The porphyrins can form a template on which RNA and DNA can form generating viroids. The porphyrins can also form a template on which prions can form. They all can join together - RNA viroids, DNA viroids, prions - to form primitive archaea. Thus the archaea are capable of self replication on porphyrin templates. The self replicating archaea can sense gravity which gives rise to consciousness. They can also sense the anti-gravity fields which gives rise to the unconscious brain. Thus there can be both self replicating archaea and anti-archaea regulating the conscious and unconscious brain. Thus the climate change stress mediated increased porphyrin synthesis leads to prefrontal cortex atrophy, cerebellar dominance, cerebellar cognitive affective disorder, quantal perception and neanderthalisation of the population. The porphyrions are self replicating supramolecular organisms which forms the precursor template on which the viroids, prions and nanoarchaea originate. Stress induced template directed abiogenesis of porphyrions, prions, viroids and archaea is a continuous

process and can contribute to changes in brain structure and behavior as well as disease process.

Endomyocardial fibrosis along with the root wilt disease of coconut is also endemic to Kerala with its radioactive actinide beach sands. Actinides like rutile, endogenous digoxin as well as organisms like phytoplasmas and viroids have been implicated in the etiology of these diseases.¹⁻⁴ Endogenous digoxin has been related to the pathogenesis of schizophrenia, malignancy, metabolic syndrome x, autoimmune disease and neuronal degeneration.⁴ The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered.⁵⁻⁸ An actinide dependent shadow biosphere of archaea in the above mentioned disease states is described.^{7,9}

Materials and Methods

The following groups were included in the study:- endomyocardial fibrosis, Alzheimer's disease, multiple sclerosis, non-Hodgkin's lymphoma, metabolic syndrome x with cerebrovascular thrombosis and coronary artery disease, schizophrenia, autism, seizure disorder, Creutzfeldt Jakob's disease and acquired immunodeficiency syndrome. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacin and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond.¹⁰ Aliquots were withdrawn at zero time immediately after mixing and after

incubation at 37 °C for 1 hour. The following estimations were carried out: - Cytochrome F420 and digoxin.¹¹⁻¹³ Cytochrome F420 was estimated fluorimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

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

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

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

Table 2. Effect of rutile and antibiotics on digoxin.

| Group | Digoxin (ng/ml) (Increase with Rutile) | | Digoxin (ng/ml) (Decrease with Doxy+Cipro) | |
|---------|---|------|---|-------|
| | Mean | ±SD | Mean | ±SD |
| Normal | 0.11 | 0.00 | 0.054 | 0.003 |
| Schizo | 0.55 | 0.06 | 0.219 | 0.043 |
| Seizure | 0.51 | 0.05 | 0.199 | 0.027 |
| AD | 0.55 | 0.03 | 0.192 | 0.040 |
| MS | 0.52 | 0.03 | 0.214 | 0.032 |
| NHL | 0.54 | 0.04 | 0.210 | 0.042 |
| DM | 0.47 | 0.04 | 0.202 | 0.025 |
| AIDS | 0.56 | 0.05 | 0.220 | 0.052 |
| CJD | 0.53 | 0.06 | 0.212 | 0.045 |
| Autism | 0.53 | 0.08 | 0.205 | 0.041 |
| EMF | 0.51 | 0.05 | 0.213 | 0.033 |
| F value | 135.116 | | 71.706 | |
| P value | < 0.001 | | < 0.001 | |

Discussion

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

Archaeal digoxin induced redox stress can produce histone deacetylase inhibition resulting in endogenous retroviral (HERV) reverse transcriptase and integrase expression. Digoxin can cut and paste the HERV RNA by modulating RNA splicing generating RNA viroidal diversity.¹⁸ This can also integrate the HERV RNA complementary DNA into the noncoding region of eukaryotic non coding DNA using HERV integrase.¹⁹ The noncoding DNA is lengthened by integrating HERV RNA complementary DNA with the integration going on as a continuing event. The archaea genome can also get integrated into human genome using integrase as has been described for trypanosomes.²⁰ The integrated archaea can undergo vertical transmission and can exist as genomic parasites.^{19, 20} This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters as well as eukaryotic speciation and individuality.²¹ The HERV RNA complementary DNA can function as jumping genes producing a dynamic genome important in storage of synaptic information, HLA gene expression and developmental gene expression. The HERV RNA can regulate mrna function by RNA interference.¹⁸ The phenomena of RNA interference can modulate T cell and B cell function,

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

The archaeal digoxin can regulate the nervous system including the NMDA/GABA thalamo-cortico-thalamic pathway mediating conscious perception.^{4, 22} NMDA/GABA receptors can be modulated by digoxin induced calcium oscillations resulting NMDA/GAD activity induction.⁴ The dipolar PAH and archaeal magnetite in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated frohlich model superconducting state²² inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world.^{4, 22} The higher degree of integration of the archaea into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance.⁴ The increased integration of archaea into the neuronal genome can produce increased digoxin mediated NMDA transmission producing schizophrenia and autism. Digoxin induced calcium oscillations can activate NFkB producing immune activation and cytokine secretion. The archaeal digoxin induced chronic immune activation can lead on to autoimmune disease.²³ Archaeal digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFkB producing the Warburg metabolic phenotype.²⁴ There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics and metabolic syndrome. The archaeal digoxin generated cytokines can lead to TNF alpha induced insulin resistance and metabolic syndrome x. Digoxin induced sodium potassium ATPase inhibition can lead to increase in HMG CoA reductase activity and increased cholesterol synthesis. The increased cholesterol substrate also leads to increased archaeal growth and digoxin synthesis due to metabolic channeling to the mevalonate pathway. Digoxin can produce sodium potassium ATPase inhibition and inward

movement of plasma membrane cholesterol. This produces defective SREBP sensing, increased HMG CoA reductase activity and cholesterol synthesis. The digoxin induced inward movement of plasma membrane cholesterol can alter membrane cholesterol/sphingomyelin ratio producing modified lipid microdomains. The digoxin induced lipid microdomain modulation can regulate the GPCR couple adrenaline, noradrenaline, glucagon and neuropeptide receptors as well as protein tyrosine kinase linked insulin receptor. The digoxin mediated inhibition of nuclear membrane sodium potassium ATPase can modulate nuclear membrane lipid microdomains and steroidal/thyroxine DNA receptor function. Thus endogenous digoxin can modulate all the endocrine receptors by regulating lipid microdomains. Hyperdigoxinemia is important in the pathogenesis of atherogenesis and metabolic syndrome x. Digoxin induced sodium potassium ATPase inhibition results in an ATP sparing effect. Eighty percent of the ATP generated is used to run the sodium potassium ATPase pump. The digoxin inhibition of the sodium potassium ATPase spares this ATP which is then used for lipid synthesis. Thus endogenous digoxin and the shadow biosphere generated Warburg phenotype can produce increased lipid synthesis and obesity important in metabolic syndrome x. Fat fuels insulin resistance by binding to the toll receptor and producing immune activation and immune infiltration of the adipose tissue. The archaeal digoxin induced monocyte activation and Warburg phenotype induced increased cholesterol synthesis leads to atherogenesis. The Warburg phenotype induced increased mitochondrial PT pore hexokinase can lead on to malignant transformation. The digoxin induced increased intracellular calcium can lead to PT pore dysfunction, cell death and neuronal degeneration.⁴ The digoxin mediated transcribed HERV RNA can get encapsulated in microvesicles contributing to the retroviral state. The prion protein conformation is modulated by HERV RNA binding producing prion disease. The archaeal digoxin and rutilone induced magnesium depletion can lead

MPS deposition and produce EMF, CCP, MNG and mucoid angiopathy.⁴ Thus the archaeal digoxin can produce neuro-immune-metabolic-endocrine-genetic integration. The increased archaeal cholesterol catabolism and digoxin secretion can lead to diverse pathological states of neuronal degeneration, metabolic syndrome x, autoimmune disease, malignancy and psychiatric disorders.

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