Chapter 3

Isoprenoid Pathway Dysfunction in Human Male Infertility

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.

Thus the actinidic archaeal symbiosis results in neanderthalisation of the population and generation of androgyny. The actinidic archaeal overgrowth and symbiosis is a consequence of global warming. Archaea are extremophiles and increase in density during periods of climate change. The actinidic archaeal catabolism of cholesterol generates digoxin and increased intracellular calcium

resulting in formation of excess of gasotransmitters important in autonomic function of structures like the corpora cavernosa. The cholesterol catabolism results in depletion of cholesterol and to a state of lack of sex hormone synthesis. This produces an asexual state resulting in a social system of matriarchy related to androgyny. The actinidic archaeal cholesterol catabolism generates porphyrins producing the extrasensory quantal perceptive state associated with androgyny. This contributes to the creativity of the androgynous state. The porphyrin synthesis associated with androgyny also contributes to the disease states associated with it. This includes autoimmune disease, cancer, degenerations, acquired immunodeficiency syndrome, metabolic syndrome X and all civilisational disease.

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

The isoprenoid pathway is a key regulatory pathway in the cell. The important metabolites of the isoprenoid pathway are digoxin (endogenous membrane Na^+-K^+ ATPase inhibitor), dolichol (important in N-glycosylation of proteins), ubiquinone (important membrane antioxidant), and cholesterol (a component of cellular membranes). The hypothalamus has been reported to produce the endogenous membrane Na^+-K^+ ATPase inhibitor digoxin. Digoxin, being a steroidal compound, is synthesized by the isoprenoidal pathway. Membrane Na^+-K^+ ATPase inhibition has been reported to lead to hypomagnesemia. Another component of the isoprenoid pathway, ubiquinone, is a free radical scavenger and component of the mitochondrial electron transport chain. The alteration in mitochondrial function and qualitative changes in membrane glycoconjugates can alter sperm motility and function. The isoprenoidal pathway was assessed in human male infertility. Systemic diseases have beep correlated with hemispheric dominance. Therefore, the isoprenoid pathway was also assessed in right hemispheric dominant, left hemispheric dominant, and bihemispheric dominant individual to assess the role of

hemispheric dominance in the genesis of human male infertility. The results are presented in this paper.

Materials and Methods

Informed consent was obtained from all the patients and normal individuals included in the study. The permission of the ethics committee of the institute was also obtained. Fifteen cases of healthy young infertile oligospermic males with defective sperm motility (less than 10% motility) between the ages of 25 and 35 years were chosen for the study. Fifteen cases each or right hemispheric, left hemispheric, and bihemispheric dominant individuals selected by the dichotic listening test were also chosen for the study. Fifteen cases of age-and sex - matched bihemispheric dominant male healthy fertile controls with normal sperm count and motility were also chosen. None of the subjects studied was under medication at the time of removal of blood. All subjects chosen for the study were nonsmokers (active or passive). Fasting blood was removed in citrate tubes from each of the patients mentioned above. RBCs were separated within I h of collection of blood for the estimation of membrane Na^+-K^+ ATPase. Plasma was used for the analysis of various parameters. The methodology used in the study was as follows: all biochemicals were obtained from Sigma Chemicals (USA). Activity of HMG CoA reductase of the plasma was determined by the method of Rao and Ramakrishnan by determining the ratio of HMG CoA to mevalonate. For the determination of the RBC Na^+-K^+ ATPase activity of the erythrocyte membrane, the procedure described by Wallach and Kamat was used. Digoxin in the plasma was determined by the procedure of Arun et al. For the estimation of ubiquinone and dolichol in the plasma, the procedure by Palmer et al was used. Magnesium in the plasma was estimated by atomic absorption spectrophotometry. Tryptophan was estimated by the method of Bloxam and Warren and tyrosine by the method of Wong and

O'Flynn. Serotonin was estimated by the method of Curzon and Green and catecholamines by the method of Well-Malhebe. Quinolinic acid content of plasma was estimated by HPLC (C_{18} column micro Bondapak 4.6 x 150 mm), solvent system 0.01 M acetate buffer (pH 3.0) and methanol (6:4), flow rate 1.0 ml/min, and detection UV (250 nm). Morphine, strychnine, and nicotine were estimated by the method described by Arun et al. Details of the procedures used for the estimation of total and individual GAG, carbohydrate components of glycoporteins, activity of enzymes involved in the degradation of GAG (β-glucuronidase, β-N-acetyl hexosaminadase, hyaluronidase, and cathepsin-D), and activity of glycohydrolases (β-galactosidase, β-fucosidase, and β-glucosidase) are as described by Manoj and Kurup. Serum glycolipids were estimated as described in methods in enzymolgoy. Cholesterol was estimated by using commercial kits supplied by Sigma Chemicals SOD was assayed by the method of Nishikimi et al. as modified by Kakkar et al. Catalase activity was estimated by the method of Maehly and Chance, glutathoine peroxidase by the method of Paglia and Valentine as modified by Lawrence and Burk, and glutathione reductase by the method of Horn and Bums. MDA was estimated by the method of Will and conjugated dienes and hydroperoxides by the procedure of Brien. Reduced glutathoine was estimated by the method of Beutler et al. Nitric oxide was estimated in the plasma by the method of Gabor and Allon. Statistical analysis was done by ANOVA.

Results

HMG CoA reductase activity, serum digoxin, and dolichol were increased in infertile human males, indicating upregulation of the isoprenoid pathway but serum ubiquinone, RBC sodium-potassium ATPase activity, and serum magnesium were reduced. The concentration of tryptophan, quinolinic acid,

strychnine, nicotine, and serotonin was higher in the plasmas of infertile men, while that of tyrosine, dopamine, morphine, and norepinephrine was lower.

There was an increase in the concentration of serum total GAC, glycolipids (ganglioside, glycosyl diglyceride, cerebrosides, and sulphatides) and carbohydrate components of glycoproteins (hexose, fucose, and sialic acid) in infertile men. The increase in the carbohydrate components - total hexose, fucose, and sialic acid - in infertile human males was not to the same extent, suggesting qualitative change in glycoprotein structure. The individual GAG fractions in the serum also showed an increase in infertile human males. The activity of GAG degrading enzymes (β-glucuronidase, β-N-acetyl hexosaminidase, hyaluronidase and cathepsin-D) and that of glycohydrolases (β-galactosidase, β-fucosidase, β-glucosidase increased significantly in the serum in infertile men.

The cholesterol: phospholipid ratio of the RBC membrane increased in infertile men. The concentration of total GAG, hexose, and fucose content of glycoprotein decreased in the RBC membrane and increased in the serum suggesting their reduced incorporation into the membrane and defective membrane formation in infertile men.

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 infertile men. The activity of enzymes involved in free radical scavenging, like superoxide dismutase, catalse, glutathione peroxidase, and glutathoine reductase, is decreased in infertile men.

HMG CoA reductase activity, serum digoxin, and dolichol were increased and ubiquinone was reduced in left-handed/right hemispheric dominant individuals. HMG CoA reductase activity, serum digoxin and dolichol were

decreased and ubiquinone was increased in right-handed/left hemispheric dominant individuals. The concentration of tryptophan, quinolinic acid serotonin, strychnine, and nicotine was found to be higher in the plasma of left-handed/right hemispheric dominant individuals, while that of tyrosine, dopamine, morphine, and norepinephrine was lower. The concentration of tryptophan, quinolinic acid serotonin, strychnine, and nicotine was lower in the plasma of right handed / left hemispheric dominant individuals, while that of tyrosine, dopamine, morphine, and norepinephrine was higher.

Discussion

Archaeal digoxin and membrane Na^+-K^+ ATPase inhibition in relation to Infertility

The archaeaon steroidelle DXP pathway and the upregulated pentose phosphate pathway contribute to digoxin synthesis. The present study shows an upregulated isoprenoid pathway in infertile human males with increased digoxin and dolichol and reduced ubiquinone, magnesium, and RBC membrane Na^+-K^+ ATPase activity. The study demonstrates that all these factors are due to an upregulated isoprenoid pathway. The increase in endogenous digoxin, a potent inhibitor of membrane Na^+-K^+ ATPase, can decrease this enzyme activity. There is increased synthesis of digoxin as evidenced by increased HMG CoA reductase activity. Studies in our laboratory have demonstrated that digoxin is synthesized by the isoprenoid pathway. In infertile human males, there was significant inhibition of the RBC membrane Na^+-K^+ ATPase activity. 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 further inhibition of Na^{+}-K^{+} ATPase, since ATP-Mg^{++} complex is the actual substrate for this reaction. Cytosolic free calcium is normally buffered by two mechanisms, ATP dependent calcium extrusion from 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 is 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 infertility in human males. Serum Mg^{++} was assessed in infertile men and was found to be reduced.

Increased digoxin levels can lead to membrane Na^{+}-K^{+} ATPase inhibition and a reduction in intracellular magnesium and to an increase in intracellular calcium in the vascular smooth muscle cell. This can lead to vasospasm and ischemia of the tubules.

Archaeal Digoxin and Regulation of Neurotransmitter Synthesis and Function in Relation to Infertility

The archaeaon neurotransminoid shikimic acid pathway contributes to tryptophan and tyrosine synthesis and catabolism generating neurotransmitters and neuroactive alkaloids. There is an increase in tryptophan and its capabilities and a reduction in tyrosine and its catabolites in the serum of infertile human males. This could be due to the fact that digoxin can regulate neutral amino acid transport system with a preferential promotion of tryptophan transport over tyrosine. The decrease in membrane Na^{+}-K^{+} ATPase activity in infertile men could be due to the fact that the hyperpolarizing neurotransmitters (dopamine, morphine, and noradrenaline) are reduced and the depolarizing 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 infertile men and could predispose to their development. Quinolinic acid, an NMDA agonist, can contribute to NMDA excitotoxicity reported in schizophreniform psychosis. Strychnine, by blocking glycinergic transmission, can contribute to the decreased inhibitory transmission in schizophreniform psychosis. Recent data suggest that the initial abnormality in schizophreniform psychosis involves a hypodopaminergic state and the low dopamine levels now observed agree with this. Nicotine, by interacting with nicotinic 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 serotoninergic activity and reduced noradrenergic outflow from locus coeruleus reported earlier in schizophreniform psychosis agrees with our finding increase of serotonin and reduced noradrenaline levels. Thus the hyperdigoxinemia-induced schizophreniform state can contribute to the pathogenesis of human male infertility.

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

The archaeaon glycosaminoglycoid and fructosoid contributes to glycoconjugate synthesis and catabolism by the process of fructolysis. The elevation in the level of dolichol suggests an increased availability for N-glycosylation of proteins. In Mg^{++} deficiency the glycolysis, Citric acid cycle, and oxidative phosphorylation are blocked and more glucose 6-phosphate is channeled 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. Altered glycoconjugates of the sperm cell membrane can lead to defective spermatic penetration of the ova.

Archaeal Digoxin and Alteration in Membrane Structure and Membrane Formation in Relation to Infertility

The archaeaon steroidelle, glycosaminoglycoid and fructosoid contribute to cell membrane formation synthesizing cholesterol by the DXP pathway and glycosaminoglycans by fructolysis. The alternation 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 an increase in intracellular calcium activating phospholipases A_2 and D. The cholesterol: phospholipid ratio of the RBC membrane was increased in infertile men. 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 cellular membrane are formed in the endoplasmic reticulum, which is then budded 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 on

GTPases and lipid knases, which are crucially dependent on magnesium and are defective in Mg^{++} deficiency. The change in membrane structure produced by an alteration in glycoconjugates and the cholesterol: phospholipid ratio can produce changes in the confomation 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. Altered spermatic cell membrane structure can lead on defective sperm motility and penetration.

Archaeal Digoxin and Mitochondrial Dysfunction in Relation to Infertility

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 decreased significantly hi most of the cases, which may be the result of low tyrosine levels, reported in infertile men 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 contributes to free radical scavenging. The increase in intracellular Ca^{++} can open the mitochondria 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 superoxide ion, which produces lipid peroidation. 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 superoxide radical to form peroxynitrite.

Increased calcium can also 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 increased intracellular calcium-related opening of the mitochondrial PT pore and outer membrane rupture. The peroxisomal membrane is defective owing to 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 human male infertility. Mitochondrial dysfunction can lead to defective sperm motility. Increased free radical generation within the sperm cell can lead to cytotoxicity and sperm destruction.

Cell death is also mediated by increased intracellular calcium and ceramide-related opening of the mitochondrial PT pore, causing a collapse of the hydrogen gradient across the inner membrane and an uncoupling of the respiratory chain. This also leads to volume dysregulation of mitochondria, causing hyperosomolality of matrix and expansion of the matrix space. The outer membrane of the mitochondria ruptures and releases AIF (apoptosis inducing factor) and cyto C (cytochrome C). This results in procaspase-9 activation to caspase-9, which produces cell death. Caspase-9 activates CAD (caspase activated deoxyribonuclease), which cleaves the nuclear membrane lamins and several proteins involved in cytoskeletal regulation like gelsolin,

which cleaves actin. Apoptosis has also been implicated in sperm death in human male infertility.

Archaeal Digoxin and Hemispheric Dominance in Relation to Infertility

The archaeaon related organelle - steroidelle, neurotransminoid and vitaminocyte contribute to hemispheric dominance. The neurotransmitter patterns and upregulated isoprenoid pathway noted in human male infertility are similar to those obtained in right hemispheric dominant individuals. In right hemispheric dominant individuals the isoprenoid pathway is upregulated with hyperdigoxinemia and increased tryptophan catabolism and reduced tyrosine catabolism. In left hemispheric dominant individuals the isoprenoid pathway is downregulated with hypodigoxinemia and reduced tryptophan catabolism and increased tyrosine catabolism. Human male infertility therefore occurs in right hemispheric chemical dominance.

References

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