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# CONCEPTUAL REVIEW OF GENES IN ALBINISM: AYURVEDIC AND MODERN VIEW

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***Abstract:*** Skin is the largest organ in the body that covers the whole body externally. It is made up of three layers viz. epidermis, dermis, and hypodermis. Cells present in the epidermis are keratinocytes, melanocytes, Langerhans' cells and Merkel's cells. Due to external or internal factors, the skin gets affected and causes skin diseases like albinism etc. According to Ayurveda, albinism is a lifestyle and hereditary disease and many concepts show that modern science also considers it. The most common presentation of albinism is oculocutaneous albinism (OCA). The pathophysiology of albinism is also similar in both (ayurveda and modern science). There are 867 known genes on the X chromosome and the majority of these genes are involved in the development of tissues such as bone, neural, blood, hepatic, renal, retina, ears, cardiac, skin, and teeth. The skin, hair, exocrine glands, and anterior pituitary are formed by the ectoderm. A rare group of diseases known as ectodermal dysplasia are caused by the aberrant development of tissues derived from the ectoderm which is the one reason for albinism. Albinism is an X-linked recessive disease. In Ayurveda, albinism is a disease of kustha (skin disease) and all kustha are caused by lifestyle and hereditary factors. If bhrajak pitta is affected it can cause albinism.

***Keywords:*** - Albinism, Gene, Bhrajak Pitta, Kustha

**MODERN CONCEPT**

## I. INTRODUCTION

Skin is the largest organ in the body that covers the whole body externally. It is made up of three layers. The layers are the epidermis, dermis, and hypodermis. The layers of the epidermis are the stratum basal (the deepest portion of the epidermis), stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum (the most superficial portion of the epidermis). Cells present in the epidermis are keratinocytes, melanocytes, Langerhans' cells and Merkel's cells. Due to external or internal factors, the skin gets affected and causes skin diseases like eczema, hidradenitis suppurative, lichen planus, lupus, psoriasis, rosacea, albinism etc.

A genetic condition known as albinism or hypopigmentation of the skin, is linked to a reduction in or lack of melanin in tissues. These cases are extremely vulnerable to the damaging effects of UV radiation, as well as an elevated risk of actinic damage and skin cancer, which is inherited by the progeny. Albinism is a recessive inheritance disease associated with the X chromosome.[1]

There are 867 known genes on the X chromosome and the majority of these genes are involved in the development of tissues such as bone, neural, blood, hepatic, renal, retina, ears, cardiac, skin, and teeth. Being an X-linked recessive inheritance, it usually only shows up in men. A man who carries the mutated allele on his single X chromosome is hemizygous, i.e. he cannot pass the disorder on to his male progeny. However, all of his female offspring would be carriers. Sons of heterozygous carrier females who are healthy inherit the

disorder. Therefore, through a carrier daughter, it can be passed from afflicted males to male grandchildren (a process known as "diagonal" or "Knight's move" transmission).[2]

The most common presentation of albinism is oculocutaneous albinism (OCA). Oculocutaneous Albinism has seven varieties (OCA1 through OCA7). The most common type of albinism occurs in humans is OCA1. One reason for the total loss of eumelanin (Eumelanin is a brown-to-black pigment that is responsible for darker shades of hair, skin, and eyes) production is tyrosinase gene mutations. However, loss-of-function mutations in any kind of OCA directly hinder the synthesis of eumelanin or have an impact on the maturation of melanosomes (intracellular organelles that are uniquely generated by pigment cells in the skin and eye, where they function to synthesize and store melanin pigments), while potentially do not affect the levels of pheomelanin (Pheomelanin is a yellow-to-red pigment that contributes to lighter shades of hair, skin, and eyes).[3]

The outcome of the molecular DNA change is known as "DNA mutations," which are single nucleotide changes in an individual organism's DNA sequence. Once a mutation arises and appears in an individual, it will either become more common in the population or disappear entirely. Genetic drift and other stochastic processes, along with natural selection, determine the final fate of mutations.

## 2. PROCESSES OF MUTATION

Both endogenous and exogenous factors can cause mutations.

### 2.1 INTERNAL FACTORS (ENDOGENOUS)

1. Errors in DNA replication
2. Errors in DNA repair mechanisms
3. Base deamination
4. Oxidative DNA damage
5. Base methylation.
6. Abasic sites

### 2.2 EXTERNAL FACTOR (EXOGENOUS)

1. Ionizing radiation
2. Ultraviolet (UV) radiation
3. Alkylating agents and aromatic amines
4. Polycyclic aromatic hydrocarbons
5. Crosslinking
6. Insertional mutagenesis.[4]

## 3. PATHOPHYSIOLOGY

After gastrulation, one of the earliest stages of embryonic development that takes place in the third week following fertilization, the development of embryonic skin commences. During gastrulation, epiblast cells proliferate and migrate downward in addition to inveighing along the primitive streak. The ectoderm, mesoderm, and endoderm are the three germ layers of unique cell lineages that are formed as a result of gastrulation. Many tissues, including the olfactory epithelium, pigmented cells, epidermis, mucosal epithelium, adenohypophysis, lens, and portions of the pharyngeal arches, are derived from the ectoderm. The ectodermal neural crest is the source of the peripheral and enteric nervous systems, spiral membranes, odontoblasts, melanocytes, facial cartilage, and entero-chromaffin cells, among other structures. The skin, hair, exocrine glands, and anterior pituitary are formed by the ectoderm.[5]

A rare group of diseases known as ectodermal dysplasia (more than 200) are caused by aberrant development of tissues derived from the ectoderm, which can include the teeth, nails, hair, and glands. Although the conditions may have distinct genetic origins, they exhibit comparable traits and manifest with a range of symptoms. Clinical diagnosis is made. In addition to spontaneous mutations, chromosomal abnormalities on separate chromosomes are the cause of ectodermal dysplasia. For instance, mutations in the EDA (ectodysplasin A) gene can cause hypo hidrotic ectodermal dysplasia (HED), a condition typically passed down as an X-linked recessive trait. The reported prevalence of ectodermal dysplasia is approximately 7 out of 100000 newborns. The historical nosologically grouping of the EDs was predicated on phenotype, our understanding of the human genome and its role in development and disease has advanced providing new opportunities to recognize, that some conditions are related at the molecular level. Information from several domains, such as phenotype, mode of inheritance, causal gene, OMIM (Online Mendelian Inheritance in Man), and molecular pathway or structure, are included in the proposed ED classification system. Based on phenotype, molecular pathway, and genotype, conditions are categorized. The most prevalent form of albinism,

known as oculocutaneous albinism type 1 (OCA1), is brought on by bi-allelic mutations (missense, nonsense, or frameshift) in the TYR gene on chromosome 11q14.3. It affects roughly 1 in 40,000 people worldwide (total OCA – 1:17,000). Most cases of this kind of albinism are found in Caucasians. (OMIM # 203100).[6]

The symptoms of X-linked inherited ocular albinism type 1 (OA1) include reduced vision, congenital nystagmus, foveal hypoplasia, and hypopigmentation of the fundus and iris. Mutations in the G protein-coupled receptor143 (GPR143) gene are the root cause of it. Data are found that phenotypes and genotypes in GPR143 in Asians, and highlight the phenotypic heterogeneity in OA1. OCA1: Autosomal recessive. Normally, L tyrosine is hydroxylated to L-DOPA and L-DOPA is oxidized to DOPA quinone by the TYR gene product tyrosinase. This acts as the melanin synthesis rate-limiting step. Lack of this function prevents the body from producing melanin.[7]

It is known that a wide range of factors, such as hormones, cytokines, and ultraviolet radiation (UVR), control the production of melanin. Although there is plenty of data available in this volume regarding cytokine responses to various stresses, including exercise and infection, relatively few studies have been published thus far (Gallagher and Daly, 1993; Grimble, 1995; Harbige, 1996). It makes sense to believe that, similar to other physiological systems, the cytokines—which function as the immune system's hormones—would be broadly impacted by nutritional status. Chronic nutritional deficiencies, for instance, harm the immune response and lower cytokine production and activity. On the other hand, little is known about whether there would be a threshold effect, whereby cytokines would abruptly stop being produced at a certain level of nutritional deficit, or whether cytokine deficits would happen gradually as nutritional adequacy becomes limiting.[8]

**AYURVEDIC CONCEPT**

**4. INTRODUCTION**

In Ayurveda, there are many concepts that can change the lifestyle of human beings. Human life starts from the embryo and undergoes many changes till death. According to Ayurveda, the body is formed by the combination of sukra (sperm) and shonit (ovum).[9] Other factors that affect the garbh dharan (conception) are ambu (nutrition), kshetra (site of conception) and kala (right time of conception).[10]

Despite these factors body is more affected by the ratio of vata, pitta and kapha in sukra and shonit. This ratio affects the phenotype and genotypes of the body. Prakriti which is a combination of genotype and phenotype remains unchanged throughout the life of an individual, but due to lifestyle modifications with time, mutation in genetic material is found in certain cases. This may be shown in the individual or their offspring (depending upon the domination of genetic material).[11]

In Ayurveda pitta dosha is responsible for pigmentation. There are five pittas, among them the pigmentation of the skin depends upon the bhrajak pitta and paachak pitta. Acharya Sushruta mentioned that bhrajak pitta present in twak, which helps in the absorption of abhyanga (massage), pareeshek (sprinkling of medicated drugs), lepa (local application) and avagaah (medicated bath) and provides Chhaya (complexion to skin, hair and other parts of the body) or Prabha (radiance of skin). Also, the pachak pitta helps in giving strength to the other four pittas (Alochak, Ranjak, Sadhak, Bhrajak).[12]

The layers of twak are formed by the maturation of Sukra-Shonit just like layers of cream on the surface of boiled milk. According to Acharya Sushruta, there are seven layers of skin. Among these the outer most layer of skin is called 'Avabhasini' which reveals all types of varna (color complexion) like Gauradi varna is reflected through Bhrajak Pitta and also illuminates shadow. The thickness of this skin is equal to one-eighteenth part of Brihi (Yava) and it is the place of Siddha and Padmakantak. The name of the second skin is 'Lohita'. Its thickness is equal to one-sixteenth of Yava and it is the place of Tilakalaka, Nyachha and Vyanga. The third skin is named 'Shweta'. Its thickness is equal to the twelfth part of barley and it is the place of diseases called Charmdal, Ajagalli and Mashak. The fourth skin called 'Tamra' is as thick as one-eighth part of barley and it is the place of various types of Kushta. The name of the fifth skin is 'Vedini' which is as thick as one-fifth of the yava. It causes Kushta and Visarp (erysipelas). The thickness of the sixth skin called 'Rohini' is equal to that of yava and it is the place of granthi, apachi, arbuda, salipad and galgand etc. The name of the seventh skin is 'Mansadhara'. It is as thick as two barley grains and causes diseases like bhagandar, arsh and vidradhi.[13]

Acharya Charak mentioned six layers of skin in the body. Like-

1. Outer skin, which holds water,
2. Holding the blood,
3. The place of origin of leprosy called Sidham and Kilas,
4. Place of origin of dadru and all kushta,
5. The place of origin of alaji and vidradhi,

When it is cut off, a man feels like a blind man entering into darkness and extremely painful arunshika with black, red, thick roots appearing on the nodes (knots) of the skin under which they are sheltered. These skin cells keep covering the entire body.[14]

## 5. PATHOPHYSIOLOGY

Abinism is a disease of kustha (skin disease) and all kustha are caused due to lifestyle and hereditary factors. Acharya Charka mentioned that use of incompatible or contrary items and drinks (excessive use of liquids), unctuous and heavy food; suppression of vomiting urge manifested after eating food and suppression of other urges as well; after exposure to heat or sun, exercise fear and immediate use (drinking) of cold water; ingesting further food even during indigestion or before digestion of previous meals; misconduct or improper management during panchakarma therapy; overuse of recently harvested cereals, curd, fish and overuse of sour (substances) and salt, masa, mulaka, pista; coitus during indigestion; day sleeping; disrespect to brahamanas and preceptors and conducting wicked or unvirtuous activities (as a result of them, one suffers from kustha).[15]

Acharya Charak also mentioned that Kustha is caused by seven morbidly impact dusya. These are vata, pitta, and kapha dosas vitiated by their respective aggravating factors; dhatus of body or dusya vitiated by morbid doshas i.e. body fluid (rasa), muscles (Mansa), blood (Sonita), and lymph (lasika). Seven varieties of kustha are produced by these morbidly affected seven dusya (three dosas & four dhatus). These manifesting with these sources, afflict the entire body.[16]

Acharya Charka mentioned that if any portion of the beeja (seed-sperm and ovum) responsible for the development of a specific body part is defective, the abnormality will manifest in that part of the body, otherwise, it does not manifest (without abnormality of seed). As a result, both types of situations are observed. All indriyas (cognitive and conative organs, particularly cognitive organs) are generated or produced by atma (soul), and their presence or absence is determined by daiva (past-life deeds). Beeja (seed) denotes sperm and ovum. Specific sections of the seed are responsible for the appearance of specific main and minor body components. The progeny may or may not be comparable to the parents (depending on the beeja or its component; if aberrant, the abnormality manifests or does not). Derived from atma (soul), this term alludes to the consequence of past life deeds being carried forward by atma to this life; if the deeds were virtuous, normal sense organs develop; if unvirtuous, these may not develop. For example, if either parent has Albinism or another obstinate skin disorder (kushta), but a portion of the seed responsible for bhrajak pitta development is not damaged, the offspring will be spared from albinism, whereas if the seed is damaged, the born offspring will suffer from albinism. If the Albinism is severe and has influenced the seed of the parents, the offspring will develop manifestations of Albinism due to bhrajak pitta damage.[17]

So, if during fertilization of sperm and ovum, if beeja bhag avyava of bhrajak pitta is affected it may cause albinism. The function of pitta is just similar to enzymes so in albinism the enzyme tyrosinase gets affected. Tyrosine, which is an amino acid present in Melanin Pigments gives dark color to our skin, hair, iris of eyes and protects our skin from ultraviolet rays.

## 6. ROLE OF EPIGENETIC

As we know the genetic codes are transferred from parents to offspring through sperm (sukra) and ovum (shonita). Regulation of gene expression is divided into five levels: epigenetic, transcriptional, post-transcriptional, translational, and post-translational.

Gene modifications that are temporary and do not affect the DNA's nucleotide sequence are referred to as epigenetic regulation. This degree of regulation is achieved via inherited chemical changes in the chromosomal proteins and/or DNA.

Methylation, the act of adding methyl groups to DNA, is one instance of how DNA can be chemically modified. Methylation generally inhibits transcription. It's interesting to note that when cells split, methylation patterns might transfer. Consequently, a parent's propensity for a gene to express itself may be inherited by their child. DNA can undergo additional heritable chemical changes.

Gene expression is impacted by epigenetic modifications in several ways. Examples of epigenetic modifications are:

### 6.1. METHYLATION OF DNA

DNA is methylated by introducing a chemical group. This group is usually added to specific regions of DNA, where it obstructs the ability of proteins to bind to DNA and "read" genes. The procedure of demethylation can be used to get rid of this chemical group. Genes are normally turned "on" by demethylation and "off" by methylation.

### 6.2. ALTERATION OF HISTONES

Histone proteins are encircled by DNA. A densely packed assembly of histones blocks the DNA from being effectively accessed by proteins designed to read a gene, thereby shutting the gene "off." A gene is "turned on" when histones are loosely arranged because more DNA is exposed or not wrapped around a histone, making it

accessible to proteins that "read" the gene. Histones can have chemical groups added or subtracted to change how tightly or loosely they are packed, which can change the state of genes from "on" to "off."

### 6.3. NON-CODING RNA

Coding and non-coding RNA are made using instructions found in DNA. Proteins are created using coding RNA. By binding to coding RNA and some proteins to degrade the coding RNA so that it can no longer be used to generate proteins, non-coding RNA aids in the regulation of gene expression. Additionally, proteins that change histones to turn genes "on" or "off" may be recruited by non-coding RNA.[18]

Due to environmental and other factors, during the epigenetic phase of gene regulation if the beeja bhag avyava of bhrajak pitta present in sukra and shonita undergo mutation then it causes albinism in the individual and it may get transferred to their offspring or in the upcoming generation.

## 7. DISCUSSION

As we know line of treatment for any disease is to remove the causative factor and give the drugs according to the stage of disease. For albinism, we can start treatment before conception. For paap karma daiva vyapaashraya chikitsa is mentioned in Ayurveda. If a parent is suffering from albinism, they can do putresthi ygaya for disease-free offspring. To control beeja bhaga avyav, we can advise shodhan treatment and lepa are recommended to strengthen bhrajak pitta like bhallatak tail/ pindeetak tail/ bibhitak tail along with ash of hoof and kaliyak, agar, amrasthi, nagakesar, kanta, parad along with gomay-rasa. We can also advise ritumati parichariya and nasya karma during pregnancy time. After birth, we can maintain a lifestyle by which we can control the transformation of disease to the next generation.

Due to environmental and other factors, during the epigenetic phase of gene regulation. If the beeja bhag avyav of bhrajak pitta present in sukra and shonita undergo mutation then it causes albinism in the individual and it may get transferred to their offspring or in the upcoming generation.

## 8. CONCLUSION

The pathophysiology of albinism is nearly same in both (Ayurveda and Morden science). So, if we want that albinism should not pass from one generation to another. We should do lifestyle modification of the patients, specifical which help in regulation of epigenetic. Epigenetic regulation can change the genetic mutation and stop the transformation of albinism.

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