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REVIEW ARTICLE

Gray Hair And Haematology: A Union of Deficiency

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SUMMARY

Graying of hair is one inevitable condition of life; gray hair can start appearing on one's head or other parts of the body at one time or another, but if one lives till he or she is old, it must appear. Hair gets gray when the production of melanin, the chemical that gives hair its colour, is reduced or stopped for any of the follicles; the new hair that will grow out will no longer have color. Usually, graying comes with old age, but sometimes it starts early in some individuals based on their genes or other conditions. These conditions include vitamin B_{12}, B_9, B_6, and iron deficiencies. These elements are also essential elements required for the production of red blood cells. Red blood cells are critical cellular components of the blood and are studied in hematology. Therefore, the union of gray hair and haematology is deficiency, primarily vitamins B12, B9, B6, and iron. If not treated promptly, these deficiencies will result in anaemia, the most common blood disorder. With these elements, management and treatment of gray hair, especially premature graying, have shown a reversal of graying. Conclusively, there is a relationship between gray hair and haematology.

INTRODUCTION

Generally, there are some inevitable circumstances in life, among which is graying of hair. Hair is one of the features or attributes of mammals, the class of animals to which humans belong. Every hair on our head comprises two sections: a pole (shaft), which is the hued part we see coming out of our heads, and a root, which is the base part which keeps the hair tied down under the scalp. The root contains the follicles, which have shade (pigment) cells known as melanocytes that produce melanin, which gives hair its unique colour (1,2).

As individuals age or advance, the intensity of the melanocytes diminishes, and they begin to die, which will bring about new hair strands losing their shading or developing lighter and becoming gray, silver, and, in the long run, white (3). When a hair follicle quits making melanin, it will never again make shading strands of hair any longer. Though turning gray of hair happens at one age, it can start early (premature graying of hair). Ordinarily, it begins in the 20s in whites, mid-30s in Asians, and late 30s or 40s in Africans. Consequently, if it starts sooner than these ages among these populaces, it is viewed as premature or early graying of hair (5). There is the '50-50-50' rule

of thumb, which states that at age 50 years of age, 50 percent of the populace has at least 50 percent gray hair (4-6).

The cause for turning gray in hair is essentially aging; as one ages, there is less production of two enzymes: first, the enzyme that helps break down hydrogen peroxide, and second, the enzyme that repairs damaged hair follicles (5). The reduction of these enzymes diminishes the shade (colour), or melanin one produces. Other reasons for turning gray incorporate heredity, smoking, iron, vitamin B 12, B9, and B6 deficiencies, depression, stress, inadequate rest, not eating a balanced diet, lack of supplements, vitiligo, hypothyroidism, and other medical problems (1,4).

Vitamin B12, vitamin B6, vitamin B9, and iron deficiencies are some of the causes of graying of hair; these elements are also essential for the production of red blood cells (one of the cellular components of blood), and their deficiencies will result to different types of anaemia which is the most well-known blood disorder (a part of hematological disorders). Anemia is the leading cause of death in numerous diseases and a worldwide issue influencing around one-fourth of individuals everywhere throughout the world (7). Studies have shown the reversal of graying of hair, especially premature graying of hair, following treatment with these essential elements. Therefore, the need to diagnose and treat these deficiencies promptly among individuals having premature graying will not only result in the reversal of graying but also avert more serious health problems, such anaemia (8).

Gray Hair: Gray hair is essentially hair that has lost its normal or unique shading (colour). Studies have demonstrated that when the follicle that delivers the pigment cells fizzles or stops or diminishes production, the hair gradually changes shading and eventually turns white (9).

Hair: Hair is a protein fiber that grows from follicles found in the dermis. Hair is one of the traits described by warm-blooded animals. Besides areas of glabrous skin, the human body is covered in follicles that produce thick terminal and fine vellus hair. Most standard excitement for hair is fixated on hair growth, hair types, and hair care. Still, hair is similarly a critical biomaterial essentially made out of protein, conspicuously alpha-keratin, and can, in like manner, talk about individuals' adequacy (health) (10).

Anatomy of the Hair

The hair comprises two sections, specifically: the hair follicle, the part underneath the skin, or the bulb when pulled from the skin. This organ is situated in the dermis and keeps up stem cells, which not only re-develop the hair after it drops out but, in addition, are enrolled to regrow skin after an injury (10). The second section of the hair is the shaft (pole; which is the hard filamentous part that reaches out over the skin surface. A cross-segment of the hair shaft might be separated generally into three zones which are the cuticle, which comprises of a few layers of flat, thin cells spread out covering each other as rooftop shingles; the cortex, which contains the keratin packages in cell structures that remain roughly rod-like and the medulla, a disrupted and open region at the fiber's center (6,11,12).

Each strand of hair comprises the medulla, cortex, and cuticle (11). The innermost region, the medulla, is not always present and is an open, unstructured region. The highly structural and organized cortex, or the second of three layers of the hair, is the primary source of mechanical strength and water uptake. The cortex contains melanin, which colors the fiber based on the number, distribution, and types of melanin granules. The shape of the follicle determines the shape of the cortex, and the shape of the fiber is related to how straight or curly the hair is. Individuals with straight hair have round hair fibers. Oval and other shaped fibers are generally wavier or curly (6,11).

The cuticle is the outer covering. Its complex

structure slides as the hair swells and is covered with a single molecular layer of lipid that makes the hair repel water. The diameter of human hair varies from 0.017 to 0.18 millimeters (0.00067 to 0.00709 in). Two million small, tubular glands and sweat glands produce watery fluids that cool the body by evaporation. The glands at the opening of the hair produce a fatty secretion that lubricates the hair. Other hair follicle structures include the oil-delivering sebaceous gland, which greases up the hair, and the arrector pili muscles, which are in charge of making hairs hold up (6,10).

HAIR GROWTH AND HAIR GROWTH CYCLE

Hair development starts inside the hair follicle. The hair's main "living" segment is found in the follicle. The visible hair is the hair shaft, which displays no biochemical action and is considered "dead." The base of a hair's root (the "bulb") contains the living cells that divide and develop to assemble the hair shaft. Blood vessels supply nourishment to the cells in the hair bulb and convey hormones that adjust hair development and structure at various occasions of life. Hair develops everywhere on the outer body aside from areas of bodily fluid and glabrous skin, for example, on the palms of the hands, bottoms of the feet, nose, and lips (6,11).

In contrast to other mammals, human hair development and shedding are irregular and not occasional or cyclical. At some random time, an irregular number of hairs will be in one of three phases of development and shedding, which means hair pursues a particular growth cycle with three unmistakable and simultaneous phases (13).

Anagen: the dynamic period of the hair. The cells in the base of the hair are dividing rapidly. Another hair is shaped and pushes the club hair (a hair that has quit developing or is no longer in the anagen stage) up the

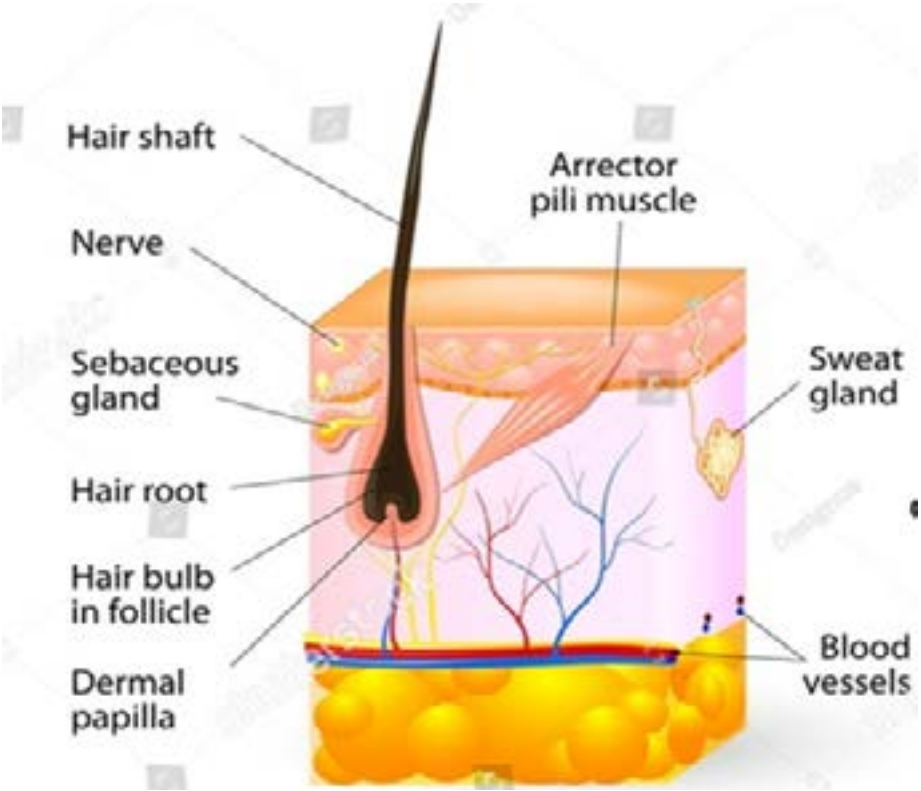

Figure 1: Parts of the Hair *Source:* Bajdek, (2015)

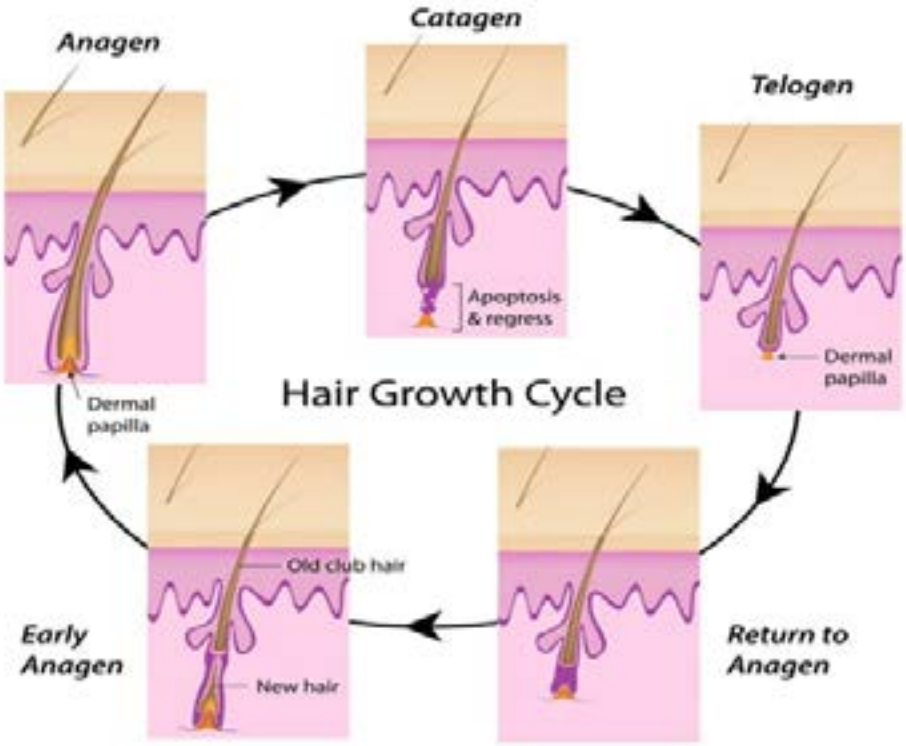

Figure 2: Hair Growth Cycle *Source:* Meng et al., (6)

follicle and, in the end, out. During this stage, the hair becomes around 1 cm every 28 days (13). Scalp hair remains in this dynamic period of development for two to six years (6,13).

The catagen phase is a transitional stage, and about 3% of all hairs are in this stage at any time. This stage goes on for around a little while (2-3 weeks). Development stops and the external root sheath shrinks and connects to the base of the hair; this is the development of what is known as club hair (13).

The telogen phase is the resting stage and ordinarily represents 6% to 8% of all hair (13). This stage goes on for around 100 days for hairs on the scalp and longer for hairs on the eyebrow, eyelash, arm, and leg (6). During this stage, the hair follicle is totally at rest and the club hair is completely framed. Hauling out hair at this stage will uncover a strong, hard, dry, white material at the root. Around 25 to 100 telogen hairs are shed regularly daily (6).

Each of the three phases of hair development happens simultaneously - while one strand of hair might be in the anagen stage, another might be in the telogen stage (13). Each has explicit qualities that decide the length of the hair. Hair develops at various rates in various individuals; the average rate is around 0.3 to 0.4 millimeters daily, one-half inch every month, and six inches each year (6). Hair shading is made by pigment cells delivering melanin in the hair follicle. Shade cells reduce or die with aging, and hair turns gray, silver, and finally white (6,13).

MELANOGENESIS (SYNTHESIS OF MELANIN IN THE HAIR FOLLICLE)

Melanocytes originate in neural crest melanoblasts that migrate to different destinations, including the basal layer of the epidermis and hair follicles, after the closure of the neural tube (14). Their migration, proliferation, and differentiation into melanin-producing cells depend on mediators

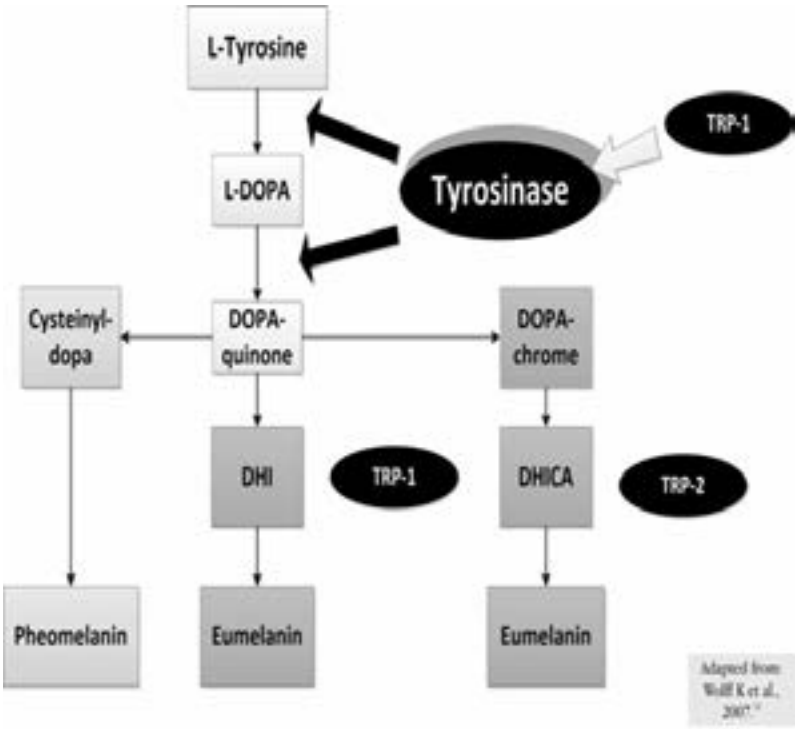

Figure 3: Melanogenesis *Source:* Wollff et al., (17)

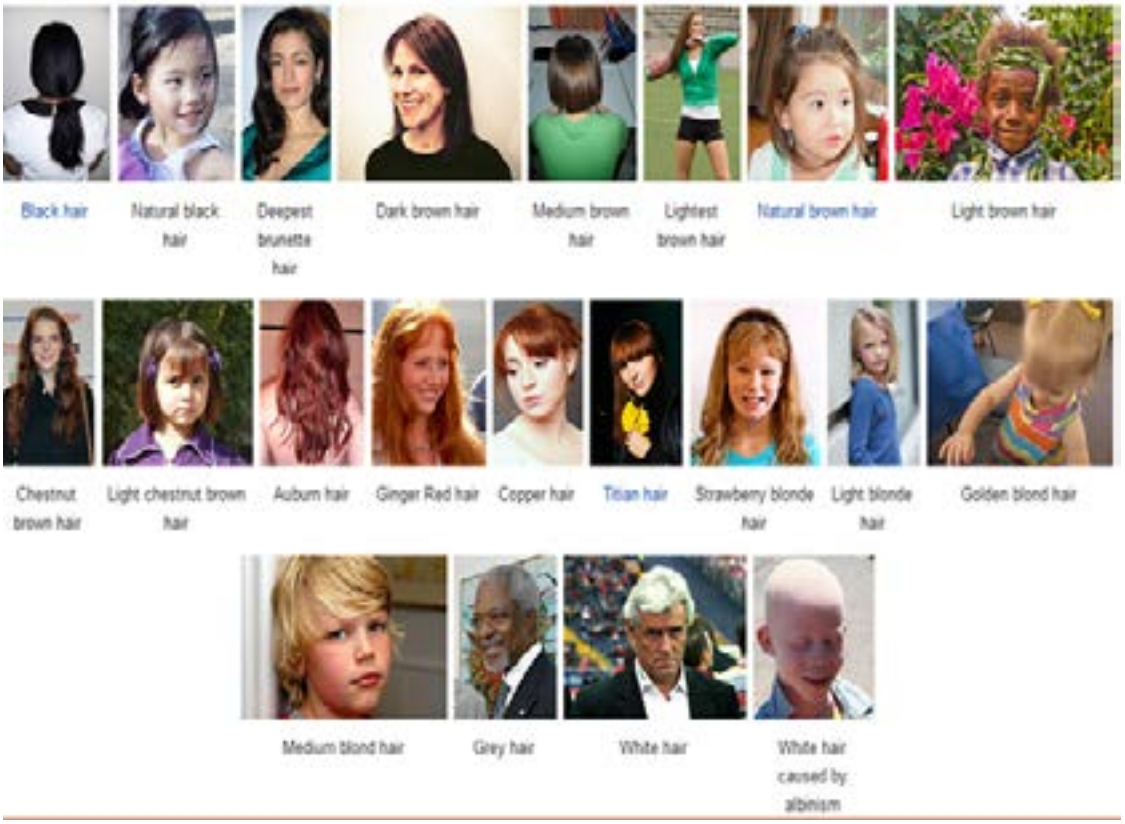

Figure 4: Shades of Hair *Source:* Anagha et al., (16)

produced by cells of the dorsal neural tube, ectoderm, and keratinocytes, such as the family of glycoproteins WNT, endothelin 3 (EDN3), and stem cell factor (SCF), which binds the c-Kit receptor tyrosine kinase in melanocytes and melanoblasts ((14). Bone morphogenic proteins antagonize these events, reducing their expression in melanocyte migration (14).

Melanin synthesis is a complex process, and it begins with the hydroxylation of the amino acid tyrosine to L-3,4-dihydroxyphenylalanine (DOPA) in a reaction catalyzed by tyrosinase. The conversion of DOPA to DOPAquinone is also catalyzed by tyrosinase. Eumelanin is synthesized in the absence of cysteine or glutathione through a spontaneous reaction or one that requires dopachrome tautomerase (DCT, formerly known as tyrosinase-related protein two or TYRP2). DOPAquinone undergoes spontaneous oxidation to produce DOPAchrome, which is, in turn, targeted by DCT to produce dihydroxycarboxylic acid. Pheomelanin is produced when DOPAquinone is loaded with cysteines. Other than tyrosinase, the remainder of the reactions are spontaneous and do not require additional catalysts (15).

After melanin is produced, it is transferred to the keratinocytes in the hair shaft. An individual can have either of the two types of melanin or a combination of both, which gives the hair different shades (16).

Formation of Gray Hair

Gray hair, also known as canities, appears when the melanocytes in the hair follicles produce less (hypopigmentation) or even stop producing (depigmentation) melanin, the pigment that gives hair its colour (1,2). Without melanin, new hair strands develop in lighter and take on different shades of gray, silver, and eventually white (5). Hypopigmentation or depigmentation may be because of a decreased melanin synthesis due to a defect in tyrosinase's structure or tyrosinase inhibition; melanin transfer from the melanocyte to the keratinocyte is obstructed, and melanosome destruction occurs or even deficiencies of some substances required for melanin production (1,2,15).

Gray hair normally begins in the 40s in the African (Nigeria) populace, but there are many cases of gray hair commencement in people under 40, and such a condition is termed premature hair graying (PHG) (3). It is said to occur more among females than males because of what females face on a daily basis, especially domestic violence. In men, it affects more of those who are financially down, making them look older (12).

Causes of Gray Hair

Gray hair was previously known to occur due to aging and genes. Today, however, it is clear that there are several other causes of gray hair, especially premature graying. The pathogenesis of premature canities is not yet clear, but various hypotheses have been suggested, including alteration in pH and cysteine levels in melanosomes, the role of trace metal ions, vitamin B12 and folic acid, vitamin D3, and oxidative stress (18). Below are some of the causes of gray hair.

Aging

All metabolic activities in the body decrease with age; one significant cause for the turning gray of hair is just maturing; as one grows older, there is less production of two enzymes: the first enzyme is catalase, which helps break down hydrogen peroxide. Hydrogen peroxide is a notable hair-bleaching agent. The hair cells produce hydrogen peroxide and accumulate due to aging, eventually fading hair color (5). Secondly, there is a decrease in the generation of the enzyme Janus kinase that helps fix harmed hair follicles; this slows down and lessens the pigment or melanin that is produced and, in the long run, results in graying of the hair (3). In addition, there is a reduction in the activity of the enzyme dopachrome tautomerase with age.

Heredity (Gene)

Qualities directly relate to how early and how rapidly silver hair happens in a person. So if both of one's folks had a full head of silver hair in their 30s, there is a probability that that individual will likewise have it at that age (5). Premature graying of hair is mainly due to genes. There is one gene that has been targeted called interferon regulatory factor 4 (IRF4), which is important in regulating and producing melanin in the hair. Mutation in this gene is associated with gray hair. Inherited in an autosomal-dominant manner. According to one theory, at least two gene pairs control human hair colour

Ethnicity

Gray hair begins at different ages (years) among different populations (ethnic groups). In the whites, it starts in their 20s, in the Asians in their 30s, and in Africans in their 40s; that is to say, the whites tend to go gray earlier (the red hairs earliest), followed by the Asians and then the Africans (5,6). The reason for these occurrences is basically the content and type of melanin in the hair of these different populations. Eumelanin (dark pigment) is significantly higher in African hair, followed by Asian and then Caucasian hair (6).

Smoking

Smoking is an inclining factor in a few illness conditions. Illuminating influences the body from head to toe and includes the hair on the head. One examination demonstrated that smokers are 21/2 times more likely to go gray before age 30 than nonsmokers and can additionally make silver dark look yellow (3). Smoking causes the release of oxidants (oxygen-reactive species) that are capable of damaging the cells of the hair follicles (melanocytes), thereby reducing the amount of melanin produced (19).

Stress

Stress does not straightforwardly cause gray hair, yet it can cause a condition that makes the hair shed around multiple (3 times) times quicker than normal. At that point there is plausibility that when the hair develops back, it will be gray rather than the unique shading (3). Oxidative stress causes imbalances when antioxidants are not enough to counteract the damaging effect of free radicals. So when oxidative stress is accumulated, it will lead to an increased amount of free radicals (oxidative reactive species), which will damage the melanocytes, thereby resulting in a reduced amount of melanin (3,19).

Nutritional Deficiencies

Some essential elements are needed for normal melanogenesis that the body does not produce but gets from diets; these elements include iron, vitamin B12, B9, B6, and even more (20).

Vitamin B12, B9 and B6 Deficiencies

These water-soluble vitamins perform important functions in the body. They are required for normal red blood cell production, repair of tissues and cells, and synthesis of DNA. Vitamin B12 is also important for normal nerve cell function (20). The recommended amounts of vitamin B12, B9, and B6 for adults are 2.4 mcg, 400.0 mcg, and 1.3 mg, respectively, and those for children are 1.8 mcg, 300.0 mcg, and 1.0 mg (21).

Cells of the hair follicle are rapidly dividing cells, and the proliferation of the cells is dependent upon the synthesis of DNA and, therefore, on a sufficient supply of vitamin B12, folic acid, and vitamin B6. Vitamin B12 stabilizes the initial anagen phase of the hair follicle. So, if these substances are deficient, the melanin production will be altered ((21).

Iron Deficiency

Iron levels affect hair melanogenesis. Iron has a significant role in tyrosinase activity, an enzyme located in melanocytes, which are specialized cells that produce melanin pigment in skin, hair, and eye color. Therefore, if an individual is low in iron, this could potentially affect tyrosinase. This, in turn, leads to hair discoloration or graying.

Daily iron requirement for women is about 18mg/day for ages 19- 50 years; however, up to 27mg for pregnant women, then older than 50 years and not menstruating 8mg/day and 8.0mg/day for children (7). The role of iron was reported in a tautomerization reaction by DOPAchrome tautomerase (DT). DOPAchrome can be converted to 5, 6-dihydroxyindole-2-carboxylic acid (DHICA) catalyzed by the enzyme DT. Iron is binding at the inner portion of DT (dopachrome tautomerase is a metalloenzyme with ferrous ions at its active site (18,22,23).

Health conditions

Certain health conditions can cause hair to gray. These include haematological tumors, such as Hodgkins lymphoma and thyroid disease (24), vitiligo, hypothyroidism, and medical problems, among others. In an examination by Abdel and Hossam (25), the level of grayness was related to coronary course ailment.

Effect of Chemical Hair Dyes and Hair Products

Chemical dyes and hair products, even shampoos can contribute to graying of hair (especially premature graying). Many of these products contain harmful ingredients that can decrease melanin. Hydrogen peroxide, which is in many hair dyes, is one of such harmful chemicals. Excessive use of products that bleach hair also will eventually cause white hair. Other causes of graying of hair include depression, inadequate rest, not eating a balanced diet, and lack of supplements (1,4).

Management and Treatment of Gray Hair

Graying of hair due to age and genetics cannot be reversed. In the case of premature hair graying and graying of hair due to other conditions, the treatment would be directed to the cause of the graying. The management and treatment of canities incorporate drugs, diet, lifestyle changes, hair dyes, and natural remedies. For example, graying of hair due to vitamin B12, B9, and B6, iron deficiencies, and hypothyroidism are reversed with vitamin, iron, and hormone replacement, respectively. Plucking off the gray hair may cause damage to the scalp (1,16). Several studies have proved the association of iron deficiency anemia with premature canities and reversing the canities with iron supplements oral ferrous sulfate 40mg/day (22,23). Another way to prevent premature graying is to quit smoking, which causes oxidative stress in your cells (16).

Haematology

This is the branch of medicine that studies the diagnosis, prognosis, and prevention of normal and abnormal components of blood and blood-forming organs. It is an option in medical laboratory sciences. The parts of blood incorporate the cells (red blood cells, white blood cells, and platelets) and the plasma, which contains different substances (21).

Red blood cells can transport oxygen to all parts of the body, but without them, all cells, tissues, and organs of the body cannot work appropriately. They may likewise result in the death of such organs. Therefore, it is imperative to maintain the red blood cells within average volume (the production of the red blood cells as at when due and their release to the peripheral blood); if not, there will be a reduced state known as anemia (7,26).

Anaemia

Anaemia is the reduced amount of hemoglobin or red blood cells underneath that which is typical for the sex, age, and land zone of an individual, by and large, hemoglobin levels < I3 g/dl and < I2 g/dl for males and females, respectively (7,27). It is the most widely recognized blood disorder, the primary cause of death in numerous ailments, and a worldwide issue affecting around one-fourth of individuals everywhere throughout the world (Janz et al., 2013). Generally, anemia affects kids, pregnant women, and the aged; it is likewise observed to be increasingly basic among females than males. Because of its signs and symptoms, those affected record low productivity, and additional costs found

in their medical care (27).

Main Types of Anaemia

The principal sorts of anaemia are those caused by blood loss, decreased red blood cell production, and increased red blood cell destruction.

Blood Loss: Anaemia because of blood loss can happen because of injury, for example, street auto collisions, unplanned cuts, damage, to mention but a few, and gastrointestinal bleeding as a result of ulcers (7,26).

Decreased RBC production: Anaemia due to decreased red blood cell production can occur when there is a deficiency in some essential elements needed for the production of red blood cells, for example, Vitamin B12, B9, and B6 deficiencies; iron deficiency; also caused by inheritance of blood disorders such as thalassemia (inherited blood disorder in which the body makes abnormal haemoglobin) and the problem with the bone marrow such as neoplasm of the bone marrow (26,28).

Increased RBC breakdown: Red blood cells have a normal life expectancy of 120 days. The increased destruction of these cells before 120 days will definitely result in anaemia. This condition can be brought about by hereditary disorders (sickle cell anaemia), malaria, and immune system ailments (26, 27).

Vitamin B12, B9 and B6 Deficiency Anaemias

Vitamin B12, B9, and B6 are three of the eight water-soluble vitamins in the vitamin B complex; they play essential roles in cell metabolism. Vitamin B6 plays a role in the synthesis of haemoglobin by acting as a coenzyme for the enzyme aminolevulinic acid (ALA) synthase. It also binds to two sides on haemoglobin to enhance the oxygen binding capacity of haemoglobin, vitamin B12, and B9 are also involved in the production of normal red blood cells, and they serve as co-enzymes in the convertion of methylmalonyl CoA to succinyl CoA and metabolism of 5-methyl tetrahydrofolate through methionine synthase during the synthesis of haemoglobin, maturation of erythrocyte precursors (30).

Vitamin B12, B9 (commonly called folate), and B6 deficiency anaemias occur when a lack of vitamin B12, folate, or B6 causes the body to produce abnormally large red blood cells that cannot function properly. The prevalence of these deficiencies is approximately 6-12% in adults under 60 years old and around 17% in adults above 60 years of age with macrocytic anaemia (20).

Table 1 World Health Organization Haemoglobin Threshold for Anaemia Across Age and Gender

Age and Gender	HB Threshold (g/dL)
Children (0.5 – 5 years)	11.00
Children (5 – 12 years)	11.50
Teens (12 – 15 years)	12.00
Non pregnant women (> 15 years)	12.00
Pregnant women	11.00
Men (> 15 years)	13.00

Source: WHO, (29) *Key:* HB = Haemoglobin.

Signs and Symptoms of Vitamin B12, B9 and B6 Deficiency Anaemias

Vitamin B12, B9, and B6 perform several critical bodily functions, including keeping the nervous system healthy. A deficiency in these vitamins can cause a wide range of symptoms, including extreme tiredness, a lack of energy, pins, and needles (paraesthesia), a sore and red tongue, mouth ulcers, muscle weakness, disturbed vision, psychological problems, which may include depression and confusion, problems with memory, understanding and judgment. Some of these problems can also happen if you have a vitamin B12 or folate deficiency but do not have anaemia (7,26,30).

Causes of Vitamin B12, B9 and B6 Deficiency Anaemias

There are a number of problems that can lead to a vitamin B12, B9 or B6 deficiency, including:

pernicious anemia, where the immune system of an individual attacks his/her healthy cells in the stomach, preventing the body from absorbing vitamin B12 from the diet; this is the most common cause of vitamin B12 deficiency in the UK (30). Lack of these vitamins in the diet and certain medicines, including anticonvulsants and proton pump inhibitors (PPIs), can affect how much of these vitamins the body absorbs. Vitamin B12, B9, and B6 deficiencies are more common in older people, affecting around 1 in 10 people aged 75 years or over and 1 in 20 people aged 65 (30).

Iron Deficiency Anaemia

Iron deficiency anaemia is the most common type of anaemia, which results from a lack of iron to produce new red blood cells. It is one of the anaemias caused by a decrease in the production of red blood cells and affects about a billion people. As of 2013, it killed about 183,000 people, while in 1990, there were about 213,000 deaths recorded (26,27,31).

Signs and Symptoms of Iron Deficiency Anaemia

Iron deficiency anaemia is characterized by the sign of pallor (reduced oxyhaemoglobin in skin or mucous membranes), and the symptoms of fatigue, lightheadedness, and weakness (7,27).

Causes of Iron Deficiency Anaemia

Several factors can cause iron deficiency anaemia. They include heavy monthly flow among females, gastrointestinal bleeding (basically due to the excessive non-steroidal anti-inflammatory drugs usage in men and women that have attained menopause, stomach ulcers, and gastrointestinal cancer), pregnant women because the baby needs sufficient blood, oxygen and nutrients supply there is need for extra iron, chronic kidney disease, inflammatory bowel disease, oesophagitis, schistosomiasis, trauma frequent blood donation, trauma etc. (27,31). Jeremiah and Koate, (27, 33, 34) in their study on anaemia, iron deficiency and iron deficiency anaemia among blood donors in Port Harcourt reported iron deficiency anaemia among frequent blood donors.

Diagnosis of Iron, Vitamin B12, B9 and B6 Deficiency Anaemias

Knowing some vital histories about an individual (a patient) will aid the diagnosis of iron, vitamin B12, B9, and B6 deficiency anaemias, for example, in IDA, the presence of blood in stool, long-distance runner (an athlete) or woman with heavy flow during menstruation. More will aid the diagnosis (7). Anaemia can generally be diagnosed with blood tests such as full blood count (red blood cell and its indices) performed manually or with automated analyzers; the modern versions of the latter often calculate the volume of the parameters involved and are printed. Haemoglobin levels lower than the haemoglobin threshold and the haematocrit level is diagnostic of anemia looking at the definition (7, 32).

More tests will be done to determine the cause and type of anaemia. For anaemia caused by iron deficiency, as iron starts reducing, one of the first parameters that would be out of range in full blood count will be a higher-than-normal red blood cell distribution width (RDW), indicating an increase in anisocytosis (different sizes of red blood cells). If the iron is reduced gradually, the increasing RDW usually appears even before anaemia shows (7).

Next, lower-than-normal mean cell volume (MCV) as iron gradually depletes is an indication of microcytosis (an increase in the number of smaller-than-normal red cells). Lower-than-normal mean cell volume (MCV), mean cell haemoglobin concentration (MCHC), and red blood cell morphology on visual examination of a peripheral blood smear narrow the problem to microcytic anaemia (7, 26).

The peripheral blood smear indicating iron deficiency anaemia shows many hypochromic (pale and relatively colorless) and microcytic cells. It may also show poikilocytosis (variation in shape) and anisocytosis (variation in size). With more severe iron-deficiency anaemia, the peripheral blood smear may show hypochromic pencil-shaped cells and occasionally small numbers of reticulocytes (7, 26).

Other useful tests include serum iron, total iron binding capacity (TIBC), and serum ferritin, evaluation of haemosiderinuria, hemoglobinuria, and pulmonary haemosiderosis, hemoglobin electrophoresis, and measurement of A2 and fetal hemoglobin. Laboratory tests such as stool testing, incubated osmotic fragility testing, and measurement of Lead in tissue and bone marrow aspiration are useful for establishing the etiology of IDA and excluding or establishing a diagnosis of one of the other microcytic anemias (7, 26).

For vitamin B12, B9, and B6 anaemias, there will be higher than normal mean cell volume (MCV), which indicates macrocytosis (an increase in the number of larger-than-normal red cells). Normal mean cell haemoglobin concentration (MCHC) indicates normochromic red blood cells. Ovalocytes are also seen, and hypersegmented neutrophils are hypersegmented. Visual examination of a peripheral blood smear narrows the problem to megaloblastic anaemia (7, 26).

Serum vitamin B12, B9, and B6 levels can be measured using the Enzyme-Linked Immunosorbent Assay (ELISA) method (21, 33-35). Normal ranges for serum levels of these elements are as follows: serum iron level is 55-160µg/dL (men) and 40-155µg/dL (females), serum vitamin B12 level is 200-900ng/ml, serum vitamin B9 level is 140-628ng/ml, and serum vitamin B6 is 5-50µg/dL (7, 31).

Treatment of Iron, Vitamin B12, B9 and B6 Deficiency Anaemias

Treatment of these anemias involves the use of diet, drugs, and supplements. To treat iron deficiency anemia, the cause and how severe it is first considered; depending on the knowledge of dietary changes and supplements, medicines and surgery may be used as treatment. Blood transfusion, iron injections, or intravenous iron therapy can be used in severe cases. Iron supplements such as ferrous sulfate or ferrous gluconate tablets boost iron levels in the body and are used primarily in cases that are not severe (7, 27). For vitamin B12, B9, and B6 anaemias diets, supplements and even injections are employed (20).

GRAY HAIR AND HAEMATOLOGY

Gray hair and haematology have a union of deficiency; several studies have reported the deficiency of some essential elements needed for blood production, especially red blood

cell production, among individuals with gray hair, and had recorded them as some of the causes of gray hair, particularly premature graying (20). Iron, vitamin B12, B9, and B6 deficiencies are some of the causes of the graying of hair (especially premature hair graying) and are also implicated in anemia. When anaemia occurs, there will be a low level of oxygen in the circulation, which will affect the metabolic activities of the whole body, including the decrease of melanocyte function (production of melanin) or even the death of the melanocytes. And if melanin production is reduced or stopped new, hair strands will become gray, silver and, eventually white (7, 25,).

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