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Premature Hair Graying: Underlying Contributors and Management Approaches - An Updated Literature Review

Anna Libera, *ORCID https://orcid.org/0009-0000-6806-3014*
E-mail *liberaania12@gmail.com*
Wojewódzki Szpital Zespolony w Kielcach

Julia Maria Kostro, *ORCID https://orcid.org/0009-0006-3455-2825*
E-mail *julikostro00@gmail.com*
Stefan Żeromski Specialist Hospital, Osiedle na Skarpie 66, 31-913 Kraków, Poland

Gabriela Makulec, *ORCID https://orcid.org/0009-0009-1357-1340*
E-mail *gabriela.makulec@gmail.com*
Wojskowy Instytut Medyczny, Szaserów 128, 04-141 Warsaw, Poland

Karolina Bartkewicz, *ORCID https://orcid.org/0009-0009-3082-7272*
E-mail *karolina.bartkiewicz2000@gmail.com*
Medical University of Warsaw (WUM), 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland.

Magdalena Papież, *ORCID https://orcid.org/0009-0001-6530-3198*
E-mail *magda.papiez.9@gmail.com*
Medical University of Warsaw (WUM), 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland

Zofia Jędra, *ORCID https://orcid.org/0009-0000-5449-9546*
E-mail *zjedra7@gmail.com*
Samodzielny Publiczny Szpital Kliniczny im. prof. W. Orłowskiego CMKP Czerniakowska 231, 00-416 Warsaw, Poland

Karolina Domosud, *ORCID https://orcid.org/0009-0007-4345-2188*
E-mail *karolinadomosud@gmail.com*
Wojskowy Instytut Medyczny, Szaserów 128, 04-141 Warsaw, Poland

Lizaveta Novik, *ORCID https://orcid.org/0009-0000-2181-2284*
E-mail *lnovik84@gmail.com*
Medical University of Warsaw (WUM), 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland.

Maciej Jakub Kozicki, *ORCID https://orcid.org/0009-0000-1966-0306*
E-mail *maciej.kozicki.mk@gmail.com*
Medical University of Warsaw (WUM), 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland.

Damian Zienkiewicz, *ORCID https://orcid.org/0009-0008-7263-1545*
E-mail *zienkiewicz.damian@gmail.com*
Szpital Praski pw. Przemienienia Pańskiego, Solidarności 67, 03-401 Warsaw, Poland

Corresponding Author: Anna Libera · **E-mail:** *liberaania12@gmail.com*

ABSTRACT

Background: Premature hair graying (PHG) is considered a distinct clinical entity, in which the presence of grey hairs on the scalp appears at a young age, generally before 20 years of age in individuals of European descent or slightly later, before 30 years of age in individuals of African ancestry. The etiology of premature hair graying remains multifactorial.

Aim of the study: The objective of this narrative review was to summarize the potential contributors, which may play a role in graying of the hair at the young age.

Material and methods: This comprehensive narrative literature review was conducted based on the scientific literature retrieved from the PubMed database. The analysis included original studies and case reports, which had been concentrated on the occurrence of PHG.

Results: The available literature suggests correlations between premature canities and nutrient deficiencies in cobalamin, copper, folic acid, biotin, iron, calcium, zinc, cholecalciferol. The positive association with PHG indicate also high level of oxidative stress, long-term emotional stress, tobacco smoking, genetic disorders, autoimmune diseases or just be a side effect of some medications.

Conclusions:

The etiology of PHG is multifactorial. To date no effective therapeutic method capable of reversing premature hair graying has been established, highlighting the need for further research.

Keywords: *premature hair graying, oxidative stress, emotional stress, nutrient deficiency, autoimmune disorders*

Introduction

Hair is a crucial feature of our external appearance and, when in good condition can improve self-confidence. The process of hair graying might be overwhelming and distressing at the same time. Melanocytes are the cells located in the hair follicles, which produce melanin, the pigment responsible for the individual shade of hair. When these cells are destroyed in follicles or just lose their function, melanin production is impaired, which contributes to grow out of new hair without pigmentation.

Generally, hair graying is individually conditioned and may begin at different ages however, in the European population mostly starts in the age range of 30-35 years (1).

Premature hair greying is a process whose onset if defined at different age, depending on the ethnicity. PHG is diagnosed before the age of 20 in individuals of Europe descent, before 25 in individuals of Asian descent, and before 30 in individuals of African. (2)

Furthermore, the etiology of PHG is multifactorial and remains poorly understood, and requires constant thorough research. To date, contributors such as: genetic predisposition, high level of oxidative stress, nutrients and vitamins deficiencies, smoking, ultraviolet radiation, emotional stress and systemic disease have been considered.

The effective management of PHG concerns conditions, which are linked to nutritional deficiencies, appropriate treating underlying disease such as hypothyroidism, vitiligo, anemia and the implementing various techniques, which lead to reduce stress level. In the literature have been reported potential therapeutic strategies for the management of scalp graying process, including supplementation with calcium pantothenate or para- aminobenzoic acid, the use of psoralen based photochemotherapy (PUVA) or other therapeutic interventions, however the effects of pigment restoration had been transient (3). The increasing attention has recently focused on potential therapeutic strategies involving mTORC1 inhibitors and McSCs.

Discussion of potential factors involved in the development of PHG:

1. Nutrient deficiency

Nutrition determines the baseline condition and pigmentation of healthy hair. Melanogenesis in the hair follicles, which is an essential biochemical process for the synthesis of eumelanin and pheomelanin, depends on the proper supply of several crucial vitamins and micronutrients. Cobalamin as a cofactor takes part in the synthesis of methionine, determines proper methylation and in the next stage production of S-adenosylmethionine (SAM), which enables the regulation of tyrosinase enzyme genes expression. Tyrosinase activity initiates the process of eumelanin and pheomelanin formation, which consequently determines the shade of hair. Yadav D.et al in the case control study observed that reduced level of B12 vitamin had been occurred in group of patients with PHG compared to controls. (4) Similar significant findings have been appeared in other study. (5) Sonthalia et al. also demonstrated a correlation between low B12 serum level and existence of PHG among study group of Indian population (6). Features such as folic acid, biotin was also investigated in Daulatabad D. et al research and reviled lower values in the study group compared to controls once. (5) Another essential factors which are in charge of the proper melanogenesis constitute serum iron and serum ferritin level. Iron is a crucial feature to proper functional of catalase enzyme, which reduces the accumulation of reactive oxygen species (ROS). Few studies had demonstrated significant association between lower iron serum level and PHG (5,9). Additionally in literature had been described a case report study, which presents the correlation between PHG in young

patient and iron deficiency anemia. Furthermore, in this case treatment with ferrous sulfate supplementation caused repigmentation of natural shade of hairs (6). The decreased level of calcium may cause PHG, which was reported by El-Sheikh et al. (8) The positive correlation of PHG and lower serum level of zinc was also find in some studies (10). The role of copper in melanogenesis seems to be clear as the cofactor of tyrosinase enzyme enables enzyme activation and as a result of melanin production in hair units so decreased level of copper means reduced efficiency of the melanogenesis process. (10).

In literature the lower serum vitamin D3 levels have also been reported in patients with PHG in some studies. (11,12)

2. Oxidative stress

Besides genetic factors, a major component promoting the PHG process is oxidative stress, which enhances the production of reactive oxygen species (ROS). The dominant chemical compound among ROS is hydrogen peroxide (H_2O_2). The accumulation of H_2O_2 in follicular units leads to inhibition of tyrosine and catalase enzymes activity, which impairs the melanin production. Furthermore, ROS damage melanocyte stem cells (McSCs), which maintains melanocytes differentiation and regeneration. In the condition of McSCs depletion, melanogenesis becomes impaired and contributes to grey hair development (7,13,14,15).

Solar ultraviolet (UV) radiation has also been linked to elevated level of oxidative stress and contemporaneously causes DNA damage in human body. After UV radiation exposure, the appearance of fur graying in mice was observed (16). This study highlighted also the antioxidant role of NRF2 protein. Mice with decreased NRF2 activity exhibited higher levels of oxidative stress markers, resulting in elevation of ROS and implication of graying process (16).

Another contributing factor is tobacco smoke, which incorporates substances that may accumulate in the hair units and consequently lead to increased levels of reactive oxygen species in hair follicles, therefore resulting in melanocytes damage and limit possibilities to melanin production. An additional negative effect of smoking is the reduced supply of oxygen and nutrients, because of compromised microcirculation in the scalp. The positive correlation between PHG and smoking was observed in a systemic review conducted by Babadjouni et al. (17). In another study, the authors also had reported a higher frequency of premature canities in a group of smokers compared to control group (18,19).

The emotional stress seems also to be the predisposing factor for PHG (20). Chronic stress contributes to persistent activation of the sympathetic nervous system, which results in elevated serum level of catecholamines. Hair follicles are particularly sensitive to increased levels of noradrenaline, a hormone that may disturb hair growth cycle and has an impact on hair pigmentation. Furthermore, the crucial function for appropriate hair pigmentation constitutes melanocyte stem cells (McSCs), which undergo depletion due to high level of serum norepinephrine. Elevated level of glucocorticoids also impacts on hair follicular cells by decreasing metabolic activity of melanocytes and increasing their susceptibility to oxidative stress (21,22).

3. Systemic autoimmune diseases:

a) Vitiligo

Vitiligo is an autoimmune disease in which melanocytes are destroyed by cytotoxic lymphocytes T CD8 +, whose activity increases in response to elevated level of inflammatory cytokines. Ramachandran V. et al. presented a case in of nonsegmental vitiligo in which both halo nevi and premature canities were detected concomitantly (23). Based on this case, the immunological component in pathophysiology of PHG should also be reflected.

b) Alopecia areata

In literature is described a case report presentation of adolescent patient, who had been diagnosed with alopecia areata. Following treatment, the regrowth of hair in the area that had been previously lost was depigmented. Furthermore, the absence of repigmentation was persistent (24).

c)Thyroid dysfunction

Thyroid hormones play a key role in maintaining homeostasis and overall well- being in the human body. Metabolic processes are regulated and largely dependent mainly on the serum level of triiodothyronine (T3), the concentration of which is controlled by thyroid-stimulating hormone (TSH). Serum TSH levels above the normal range are generally indicative of hypothyroidism, which is characterized by low T3 levels in blood and decreased activity of tyrosine enzyme. As the result, melanin production within hair follicles becomes less effective.

Sonthalia et al. had analyzed cases of patients with premature canities and reported a statistically significant difference in serum TSH levels. Higher TSH levels were established among people with PHG (25).

d)Pernicious anemia

This autoimmune disease is characterized by the presence of autoantibodies against intrinsic factor, which plays a primary role in the absorption of cobalamin (vitamin B12). The major function of vitamin B12 in melanogenesis was described earlier in the current article. Cases of transient PHG associated with vitamin B12 deficiency had been reported in the literature and the condition was responsive to parenteral treatment (26).

e) Hodgkin lymphoma

In literature premature canities was also described among patients with Hodgkin lymphoma and individuals infected with human immunodeficiency virus (27,28).

4. Drugs

Certain medications could also have influence on appearance of greying process.

The potential role of some drugs in induction premature canities seems to be rare, but has been established in several studies. The first group of medical substances constitute drugs used in cancer treatment such as cisplatin, anthracycline, paclitaxel, docetaxel, which by their cytotoxic effect damage melanocytes placed in the hair follicle (29). The manifestation of hair depigmentation was also observed during systemic therapy with inhibitors of programmed cell death protein 1 (PD-1) such as nivolumab, pembrolizumab, spartalizumab, ipilimumab (30,31,32). Admittedly, cases which had been found in literature not pertained to patients under the age of 30, but immunotherapy seems to be increasingly administrated, so hair hypopigmentation as an adverse effect of checkpoint inhibitors is so probable. Besides anti-PD-1 monoclonal antibodies implementation also have the potential to reverse the process of hair graying and restore their initial pigmentation through their dual immunomodulatory effects on melanocytes within scalp hair follicles (32). Similar disparity in hair pigmentation has been declared during treatment with tyrosine kinase inhibitors (TKIs). These molecularly targeted agents, acting as c-Kit antagonists, block the signaling pathway regulated by c-Kit, resulting in decrease activity of microphtalmia- associated transcription factor (MITF), which leads to downregulations of tyrosinase genes expression and impaired melanin synthesis (33,34).

Several studies revealed the occurrence of hair depigmentation in the course of imatinib, and dasatinib therapy. (35,36,37,38). The onset of depigmented hair was also reported during treatment with pazopanib. Notably, the graying process had been occurred at a relatively young age (39,40).

The association between hair depigmentation and antiepileptic drugs such as valproate, phenobarbital, phenytoin had also been reported (41,42). Additionally, several studies had suggested that antimalarial therapy based on chloroquine or hydroxychloroquine may be indicative for hair pigment disturbances (43,44).

5. Genetic conditions

Genetic disorders may also play a key role in some cases of premature canities. The first of this is Werner syndrome, which follows an autosomal recessive pattern of inheritance, and is caused by mutations in the WRN gene, responsible for genomic integrity. This genetic condition is manifests with systemic symptoms like cardiovascular disturbances, diabetes mellitus type 2, development of malignancies and primarily the occurrence of premature aging features, including PHG (45,46). Based on literature case reports, premature canities was occurred in patients in their early twenties (47,48).

Another genetic condition, which also can exert in grey hair at young age is dyskeratosis congenita. This disease entity demonstrates three patterns of inheritance: autosomal dominant, autosomal recessive and X-linked. Mutations in various genes had been identified, resulting in accelerated telomers attrition and decreed activity of telomerase enzyme. Furthermore, all these disturbances lead to sustained cells death and defects in presence of premature aging manifestation. It is associated with a triad of symptoms, which consists of nail dystrophy, oral leukoplakia and reticular skin pigmentation (49,50). Ratnasamy et al. had described a case report in which a patient with dyskeratosis congenita presented with PHG (51).

Management

The basis of PHG treatment constitutes an undergoing initial laboratory investigation, which may help identify nutritional deficiencies or hormonal disorders. In cases of vitamins and macro or microelements deficiency, appropriate supplementation should be provided. In the condition of hormonal levels irregularity or systemic autoimmune disease diagnosed, proper treatment should be initiated. Furthermore, stress may be one of the contributing factors to PHG, so reducing stress level through various relaxation techniques and regular physical activity may help to reduce the severity of premature canities. It is also advisable to limit the consumption of substances such as alcohol and tobacco. Currently, there is any approved treatment, which would be targeted for PHG.

Currently, the most effective method for dealing with gray hair remains the covering them by using semipermanent or permanent hair dyes. Unfortunately, the result is temporary and requires consistent reapplication. Frequent hair dyeing causes hair damages, dryness and requiring proper haircare and may also involves substantial costs.

Early findings in the literature suggested a potential effect on repigmentation of grey hair during supplementation of calcium pantothenate or potassium para-aminobenzoic acid (PABA). A study performed by Pasricha reviled repigmentation in some cases during treatment with 200 mg of calcium pantothenate daily (52). Hair darkening was also observed during treatment with high dose of PABA (53). In the majority, the positive effect of supplementation was temporary and the hair regrew grey after supplementation discontinuation. The downside of those studies is the fact that most of them are limited to small sample of study group. In literature it had also been reported that restoration of pigment in scalp hair occurred in some patients with PHG, who had been treated with psoralen photochemotherapy (PUVA) over a 13-month period (54).

Other potential treatment option seems to be the topical using of biomimetic peptide referred to palmitoyl tetrapeptide- 20 (PTP20), which functions as an alfa-melanin- stimulating hormone (MSH) agonist. It has been reported that PTP20 may regulate the activity of genes, involved in melanogenesis. Furthermore, it can promote the catalase activity, thereby reducing the concentration of H_2O_2 (55,56).

The available literature identifies also the topical using of a biomimetic peptide (5 % melitane), which may activate melanocortin 1 receptors (MC1R) and restore proper melanin synthesis. It has been reported a case report of 14-year-old girl, who was treated with melitane for a period of 24 months and after that a significant repigmentation of hair was reported (57). Another agent, which shown potential in reversing hair graying during long- term administration is a prostaglandin analogue- latanoprost, which has the potential to activation of melanogenesis pathway (58,59).

Based on the previous studies, anti- inflammatory drugs such as: prednisone, interferon-alfa, adalimumab, cyclosporine, acitretin, thalidomide may in some cases restore natural hair pigmentation. Moreover, imatinib, tamoxifen and dopaminergic agents have also been reported to increase melanin synthesis (42, 60).

Future promising directions seems to be therapies that will be aimed at restoration of proper physiological function of melanocyte stem-cells by enhancing their capacity for dedifferentiation and promoting cellular plasticity (61). Another interesting study conducted by Suzuki et al. presented that increased mTORC1activity contributes to decreased melanin production and impaired hair growth, therefore mTORC1 inhibitors may also become effective therapeutic approach for premature canities. (62).

Conclusions:

Hair graying is an age-related physiological process, whereas premature canities occurs before the expected age and may result from various metabolic disorders, which lead to impaired melanogenesis and an earlier onset of grey hair. The etiology of PHG is multifactorial and still requires comprehensive investigations to support the development of targeted therapies. Current limitations of the available studies and case reports include small sample size. At present, effective therapeutic approached remain limited to supplementation of iron, vitamin B12, copper in cases of deficiency, as well as restoration of a euthyroid status. Future therapeutic directions involving melanocyte stem cells or modulation of mTORC1 activity seem to be promising, however further research and clinical interventions are needed to evaluate their efficacy in hair repigmentation.

Disclosure

The authors report no disclosures.

Author's contribution

Conceptualization: Anna Libera, Julia Kostro and Karolina Bartkiewicz

Methodology: Gabriela Makulec, Karolina Domosud,

Investigation: Zofia Jędra, Magdalena Papież, Maciej Kozicki

Data curation: Magdalena Papież and Zofia Jędra, Karolina Domosud

Formal analysis: Maciej Kozicki, Damian Zienkiewicz, Lizaveta Novik

Visualization: Gabriela Makulec and Damian Zienkiewicz and Lizaveta Novik

Writing – original draft: Anna Libera, Julia Kostro and Karolina Bartkiewicz

Writing – review and editing: Anna Libera and Julia Kostro

Supervision: Anna Libera, Julia Kostro and Karolina Bartkiewicz

Project administration: Anna Libera

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REFERENCES

1. Maymone MBC, Laughter M, Pollock S, Khan I, Marques T, Abdat R, Goldberg LJ, Vashi NA. Hair Aging in Different Races and Ethnicities. J Clin Aesthet Dermatol. 2021 Jan;14(1):38-44. Epub 2021 Jan 1. PMID: 33584967; PMCID: PMC7869811.
2. Bhat RM, Sharma R, Pinto AC, Dandekeri S, Martis J. Epidemiological and investigative study of premature graying of hair in higher secondary and pre-university school children. Int J Trichology. 2013 Jan;5(1):17-21. doi: 10.4103/0974-7753.114706. PMID: 23960391; PMCID: PMC3746220.
3. Poonia K, Bhalla M. Premature Graying of Hair: A Comprehensive Review and Recent Insights. Indian Dermatol Online J. 2024 Aug 30;15(5):721-731. doi: 10.4103/idoj.idoj_807_23. PMID: 39359282; PMCID: PMC11444426.
4. A Study of Micronutrient Levels in Premature Canities in Children Yadav, Deepika; Chander, Ram; Mendiratta, Vibhu; Debnath, Ekta1; Bisherwal, Kavita; Das, Suparna Indian Journal of Paediatric Dermatology 23(4):p 297-301, Oct–Dec 2022. DOI: 10.4103/ijpd.ijpd_153_21
5. Daulatabad D, Singal A, Grover C, Chhillar N. Prospective Analytical Controlled Study Evaluating Serum Biotin, Vitamin B12, and Folic Acid in Patients with Premature Canities. Int J Trichology. 2017 Jan-Mar;9(1):19-24. doi: 10.4103/ijt.ijt_79_16. PMID: 28761260; PMCID: PMC5514791.
6. Sonthalia S, Priya A, Tobin DJ. Demographic Characteristics and Association of Serum Vitamin B12, Ferritin and Thyroid Function with Premature Canities in Indian Patients from an Urban Skin Clinic of North India: A Retrospective Analysis of 71 Cases. Indian J Dermatol. 2017 May-Jun;62(3):304-308. doi: 10.4103/ijd.IJD_221_17. PMID: 28584374; PMCID: PMC5448266.
7. Seiberg M. Age-induced hair greying - the multiple effects of oxidative stress. Int J Cosmet Sci. 2013 Dec;35(6):532-8. doi: 10.1111/ics.12090. Epub 2013 Oct 10. PMID: 24033376.
8. El-Sheikh AM, Elfar NN, Mourad HA, Hewedy ES. Relationship between Trace Elements and Premature Hair Graying. Int J Trichology. 2018 Nov-Dec;10(6):278-283. doi: 10.4103/ijt.ijt_8_18. PMID: 30783336; PMCID: PMC6369637.
9. Choi JW, Lew BL, Sim WY. A Case of Premature Hair Graying Treated with Ferrous Sulfate. Ann Dermatol. 2016 Dec;28(6):775-776. doi: 10.5021/ad.2016.28.6.775. Epub 2016 Nov 23. PMID: 27904283; PMCID: PMC5125965.
10. Yadav, Deepika; Chander, Ram; Mendiratta, Vibhu; Debnath, Ekta1; Bisherwal, Kavita; Das, Suparna. A Study of Micronutrient Levels in Premature Canities in Children. Indian Journal of Paediatric Dermatology 23(4):p 297-301, Oct–Dec 2022. | DOI: 10.4103/ijpd.ijpd_153_21

11. Bhat RM, Sharma R, Pinto AC, Dandekeri S, Martis J. Epidemiological and investigative study of premature graying of hair in higher secondary and pre-university school children. Int J Trichology. 2013 Jan;5(1):17-21. doi: 10.4103/0974-7753.114706. PMID: 23960391; PMCID: PMC3746220.
12. Kumar AB, Shamim H, Nagaraju U. Premature Graying of Hair: Review with Updates. Int J Trichology. 2018 Sep-Oct;10(5):198-203. doi: 10.4103/ijt.ijt_47_18. PMID: 30607038; PMCID: PMC6290285.
13. Wood JM, Decker H, Hartmann H, Chavan B, Rokos H, Spencer JD, Hasse S, Thornton MJ, Shalbaf M, Paus R, Schallreuter KU. Senile hair graying: H2O2-mediated oxidative stress affects human hair color by blunting methionine sulfoxide repair. FASEB J. 2009 Jul;23(7):2065-75. doi: 10.1096/fj.08-125435. Epub 2009 Feb 23. PMID: 19237503.
14. Slominski A, Wortsman J, Plonka PM, Schallreuter KU, Paus R, Tobin DJ. Hair follicle pigmentation. J Invest Dermatol. 2005 Jan;124(1):13-21. doi: 10.1111/j.0022-202X.2004.23528.x. PMID: 15654948; PMCID: PMC1201498.
15. Jo SK, Lee JY, Lee Y, Kim CD, Lee JH, Lee YH. Three Streams for the Mechanism of Hair Graying. Ann Dermatol. 2018 Aug;30(4):397-401. https://doi.org/10.5021/ad.2018.30.4.397
16. Rojo de la Vega M, Zhang DD, Wondrak GT. Topical Bixin Confers NRF2-Dependent Protection Against Photodamage and Hair Graying in Mouse Skin. Front Pharmacol. 2018 Mar 27;9:287. doi: 10.3389/fphar.2018.00287. PMID: 29636694; PMCID: PMC5880955.
17. Babadjouni A, Pouldar Foulad D, Hedayati B, Evron E, Mesinkovska N. The Effects of Smoking on Hair Health: A Systematic Review. Skin Appendage Disord. 2021 Jun;7(4):251-264. doi: 10.1159/000512865. Epub 2021 Feb 24. PMID: 34307472; PMCID: PMC8280411.
18. Sabharwal R, Gupta A, Moon N, Mahendra A, Sargaiyan V, Gupta A, Subudhi SK, Gupta S. Association between use of tobacco and age on graying of hair. Niger J Surg. 2014 Jul;20(2):83-6. doi: 10.4103/1117-6806.137308. PMID: 25191099; PMCID: PMC4141451.
19. Zayed AA, Shahait AD, Ayoub MN, Yousef AM. Smokers' hair: Does smoking cause premature hair graying? Indian Dermatol Online J. 2013 Apr;4(2):90-2. doi: 10.4103/2229-5178.110586. PMID: 23741662; PMCID: PMC3673399.
20. Thompson KG, Marchitto MC, Ly BCK, Chien AL. Evaluation of Physiological, Psychological, and Lifestyle Factors Associated with Premature Hair Graying. Int J Trichology. 2019 Jul-Aug;11(4):153-158. doi: 10.4103/ijt.ijt_43_19. PMID: 31523106; PMCID: PMC6706993.
21. Zhang B, Ma S, Rachmin I, He M, Baral P, Choi S, Gonçalves WA, Shwartz Y, Fast EM, Su Y, Zon LI, Regev A, Buenrostro JD, Cunha TM, Chiu IM, Fisher DE, Hsu YC. Hyperactivation of sympathetic nerves drives depletion of melanocyte stem cells. Nature. 2020 Jan;577(7792):676-681. doi: 10.1038/s41586-020-1935-3. Epub 2020 Jan 22. PMID: 31969699; PMCID: PMC7184936.
22. Slominski A, Wortsman J, Tuckey RC, Paus R. Differential expression of HPA axis homolog in the skin. Mol Cell Endocrinol. 2007 Feb;265-266:143-9. doi: 10.1016/j.mce.2006.12.012. Epub 2006 Dec 29. PMID: 17197073; PMCID: PMC1839836.
23. Ramachandran V, Kim KM, Zhang L. Disseminated Nonsegmental Vitiligo Associated With Halo Nevi and Premature Gray Hair. Cureus. 2021 Mar 13;13(3):e13868. doi: 10.7759/cureus.13868. PMID: 33859916; PMCID: PMC8038926.
24. Wade MS, Sinclair RD. Persistent depigmented regrowth after alopecia areata. J Am Acad Dermatol. 2002 Apr;46(4):619-20. doi: 10.1067/mjd.2002.120604. PMID: 11907522.
25. Sonthalia S, Priya A, Tobin DJ. Demographic Characteristics and Association of Serum Vitamin B12, Ferritin and Thyroid Function with Premature Canities in Indian Patients from an Urban Skin Clinic of North India: A Retrospective Analysis of 71 Cases. Indian J Dermatol. 2017 May-Jun;62(3):304-308. doi: 10.4103/ijd.IJD_221_17. PMID: 28584374; PMCID: PMC5448266.
26. Noppakun N, Swasdikul D. Reversible hyperpigmentation of skin and nails with white hair due to vitamin B12 deficiency. Arch Dermatol. 1986 Aug;122(8):896-9. PMID: 374087
27. Trakymiene SS, Abla O. Hodgkin lymphoma presenting with hair graying. J Pediatr Hematol Oncol. 2010 Jul;32(5):417-8. doi: 10.1097/MPH.0b013e3181df6172. PMID: 20502355.
28. Wadhwa SL, Khopkar U, Nischal KCValia RG, Valia RA. Hair and scalp disorders IADVL Textbook of Dermatology. 20083rd ed Mumbai Bhalani Publishing House:864–948
29. 1.Watanabe T, Yagata H, Saito M, Okada H, Yajima T, Tamai N, Yoshida Y, Takayama T, Imai H, Nozawa K, Sangai T, Yoshimura A, Hasegawa Y, Yamaguchi T, Shimozuma K, Ohashi Y. A multicenter survey of temporal changes in chemotherapy-induced hair loss in breast cancer patients. PLoS One. 2019 Jan 9;14(1):e0208118. doi: 10.1371/journal.pone.0208118. PMID: 30625139; PMCID: PMC6326423.
30. Dimitriou F, Mangana J, Dummer R. Hair Depigmentation and Hair Loss in Advanced Melanoma Treated with Combined Immunotherapy and Targeted Therapy. Acta Derm Venereol. 2020 Jan 7;100(1):adv00007. doi: 10.2340/00015555-3355. PMID: 31626322; PMCID: PMC9128868.
31. Rao H, Guo Z, Wen X, Zeng X, Wu L, Huang L. Case Report: Immune checkpoint inhibitor-related vitiligo-like depigmentation in non-melanoma advanced cancer: A report of three cases and a pooled analysis of individual patient data. Front Oncol. 2023 Jan 13;12:1099108. doi: 10.3389/fonc.2022.1099108. PMID: 36713515; PMCID: PMC9881409.
32. Rivera N, Boada A, Bielsa MI, et al. Hair Repigmentation During Immunotherapy Treatment With an Anti–Programmed Cell Death 1 and Anti–Programmed Cell Death Ligand 1 Agent for Lung Cancer. JAMA Dermatol. 2017;153(11):1162–1165. doi:10.1001/jamadermatol.2017.2106
33. D'Mello, Stacey A. N., Graeme J. Finlay, Bruce C. Baguley, and Marjan E. Askarian-Amiri. 2016. "Signaling Pathways in Melanogenesis" International Journal of Molecular Sciences 17, no. 7: 1144. https://doi.org/10.3390/ijms17071144
34. Alexeev V, Yoon K. Distinctive role of the cKit receptor tyrosine kinase signaling in mammalian melanocytes. J Invest Dermatol. 2006 May;126(5):1102-10. doi: 10.1038/sj.jid.5700125. PMID: 16410786.
35. Balagula Y, Pulitzer MP, Maki RG, Myskowski PL. Pigmentary changes in a patient treated with imatinib. J Drugs Dermatol. 2011 Sep;10(9):1062-6. PMID: 22052279.

36. Mariani S, Abruzzese E, Basciani S, Fiore D, Persichetti A, Watanabe M, Spera G, Gnessi L. Reversible hair depigmentation in a patient treated with imatinib. Leuk Res. 2011 Jun;35(6):e64-6. doi: 10.1016/j.leukres.2010.11.028. Epub 2010 Dec 19. PMID: 21176848.
37. Brazzelli V, Grasso V, Barbaccia V, Manna G, Rivetti N, Zecca M, Giorgiani G, Vassallo C, Borroni G. Hair depigmentation and vitiligo-like lesions in a leukaemic paediatric patient during chemotherapy with dasatinib. Acta Derm Venereol. 2012 Mar;92(2):218-9. doi: 10.2340/00015555-1289. PMID: 22307953.
38. Sharma V, Bagrodia V. Hypopigmentation of the Skin and Hair Associated with Dasatinib Therapy. Turk J Haematol. 2024 May 30;41(2):116-117. doi: 10.4274/tjh.galenos.2023.2023.0280. Epub 2023 Sep 12. PMID: 37698254; PMCID: PMC11589257.
39. Harrak S, Lemsanes S, Razine S, Najem S, Lkhoyaali S, Boutayeb S, et al. Rapid hair depigmentation following treatment with pazopanib for metastatic renal cell carcinoma: Case report. World J Innov Res. 2021;10:20-1.
40. Jain A, Goyal V, Soni S, Narayan S, Redhu P, Mathighatta Shivarudraiah SS, Talwar V. Hair depigmentation in a patient treated with pazopanib: A case report and a comprehensive analysis. Indian Journal of Skin Allergy. 2024;3:71–73. doi:10.25259/IJSA_52_2023.
41. Kakunje A, Prabhu A, Sindhu Priya ES, Karkal R, Kumar P, Gupta N, Rahyanath PK. Valproate: It's Effects on Hair. Int J Trichology. 2018 Jul-Aug;10(4):150-153. doi: 10.4103/ijt.ijt_10_18. PMID: 30386073; PMCID: PMC6192236.
42. Sofia M. Perez, Sarah A. AlSalman, Louise Chateaubriand Campos, Antonella Tosti, Drug-induced hair pigmentation: Clinical perspectives and updates, JAAD Reviews, Volume 3, 2025, Pages 6-17, SSN 2950-1989,
43. Di Giacomo TB, Valente NY, Nico MM. Chloroquine -induced hair depigmentation. Lupus. 2009 Mar;18(3):264-6. doi: 10.1177/0961203308097473. PMID: 19213866.
44. Schroeder RL, Gerber JP. Chloroquine and hydroxychloroquine binding to melanin: Some possible consequences for pathologies. Toxicol Rep. 2014 Nov 4;1:963-968. doi: 10.1016/j.toxrep.2014.10.019. PMID: 28962308; PMCID: PMC5598414.
45. Hürlimann AF, Schnyder UW. Werner-Syndrom mit torpiden trophischen Ulcera cruris [Werner syndrome with torpid trophic ulcera cruris]. Hautarzt. 1991 Nov;42(11):721-5. German. PMID: 1769837.
46. Davis T, Kipling D. Werner Syndrome as an Example of Inflamm-aging: Possible Therapeutic Opportunities for a Progeroid Syndrome? Rejuvenation Research. 2006;9(3):402-407. doi:10.1089/rej.2006.9.402
47. Uysal S, Demir AN, Sulu C, Kara Z, Muradov I, Kadıoğlu P. A rare case report: Werner syndrome. JCEM Case Rep. 2023 Jan 27;1(Suppl 1):luac014.029. doi: 10.1210/jcemcr/luac014.029. PMCID: PMC10653181.
48. Yamamoto K, Imakiire A, Miyagawa N, Kasahara T. A report of two cases of Werner's syndrome and review of the literature. J Orthop Surg (Hong Kong). 2003 Dec;11(2):224-33. doi: 10.1177/230949900301100222. PMID: 14676353.
49. Savage SA. Dyskeratosis congenita and telomere biology disorders. Hematology Am Soc Hematol Educ Program. 2022 Dec 9;2022(1):637-648. doi: 10.1182/hematology.2022000394. PMID: 36485133; PMCID: PMC9821046.
50. Sneha S, Sudha S, Nair RG, Dyuthi G. Dyskeratosis congenita with squamous cell carcinoma of the tongue: A rare case report. Indian J Pathol Microbiol. 2025 Jul 1;68(3):600-602. doi: 10.4103/ijpm.ijpm_846_23. Epub 2024 Jul 13. PMID: 39011607.
51. Ratnasamy V, Navaneethakrishnan S, Sirisena ND, Grüning NM, Brandau O, Thirunavukarasu K, Dagnall CL, McReynolds LJ, Savage SA, Dissanayake VHW. Dyskeratosis congenita with a novel genetic variant in the DKC1 gene: a case report. BMC Med Genet. 2018 May 25;19(1):85. doi: 10.1186/s12881-018-0584-y. PMID: 29801475; PMCID: PMC5970516.
52. Pasricha JS. Effect of Grey Hair Evulsion on the Response to Calcium Pantothenate in Premature Grey Hairs. Indian Journal of Dermatology, Venereology and Leprology. 1986 Mar-Apr;52(2):77-80. PMID: 28150658.
53. ZARAFONETIS CJ. Darkening of gray hair during para-amino-benzoic acid therapy. J Invest Dermatol. 1950 Dec;15(6):399-401. doi: 10.1038/jid.1950.121. PMID: 14794992.
54. Pavithran K. Puvasol Therapy in Premature Greying of Hair. Indian J Dermatol Venereol Leprol. 1986 Mar-Apr;52(2):74-75. PMID: 28150657
55. Chavan D. Reversal of Premature Hair Graying Treated with a Topical Formulation Containing α-Melanocyte-Stimulating Hormone Agonist (Greyverse Solution 2%). Int J Trichology. 2022 Nov-Dec;14(6):207-209. doi: 10.4103/ijt.ijt_85_22. Epub 2023 Jan 31. PMID: 37034550; PMCID: PMC10075347.
56. Almeida Scalvino S, Chapelle A, Hajem N, Lati E, Gasser P, Choulot JC, Michel L, Hocquaux M, Loing E, Attia J, Wdzieczak-Bakala J. Efficacy of an agonist of α-MSH, the palmitoyl tetrapeptide-20, in hair pigmentation. Int J Cosmet Sci. 2018 Oct;40(5):516-524. doi: 10.1111/ics.12494. Epub 2018 Oct 8. PMID: 30222197.
57. Sakhiya JJ, Sakhiya DJ, Patel MR, Daruwala FR. Case report on premature hair graying treated with Melitane 5% and oral hair supplements. Indian J Pharmacol. 2019 Sep-Oct;51(5):346-349. doi: 10.4103/ijp.IJP_166_19. Epub 2019 Nov 26. PMID: 31831925; PMCID: PMC6892010.
58. Grierson I, Jonsson M, Cracknell K. Latanoprost and pigmentation. Jpn J Ophthalmol. 2004 Nov-Dec;48(6):602-12. doi: 10.1007/s10384-004-0110-y. PMID: 15592791.
59. Bellandi S, Amato L, Cipollini EM, Antiga E, Brandini L, Fabbri P. Repigmentation of hair after latanoprost therapy. J Eur Acad Dermatol Venereol. 2011 Dec;25(12):1485-7. doi: 10.1111/j.1468-3083.2010.03949.x. Epub 2010 Dec 29. PMID: 21198953.
60. Yale K, Juhasz M, Atanaskova Mesinkovska N. Medication-Induced Repigmentation of Gray Hair: A Systematic Review. Skin Appendage Disord. 2020 Jan;6(1):1-10. doi: 10.1159/000504414. Epub 2019 Dec 17. PMID: 32021854; PMCID: PMC6995950.
61. Sun Q, Lee W, Hu H, Ogawa T, De Leon S, Katehis I, Lim CH, Takeo M, Cammer M, Taketo MM, Gay DL, Millar SE, Ito M. Dedifferentiation maintains melanocyte stem cells in a dynamic niche. Nature. 2023 Apr;616(7958):774-782. doi: 10.1038/s41586-023-05960-6. Epub 2023 Apr 19. PMID: 37076619; PMCID: PMC10132989.
62. Suzuki T, Chéret J, Scala FD, Akhundlu A, Gherardini J, Demetrius DL, O'Sullivan JDB, Kuka Epstein G, Bauman AJ, Demetriades C, Paus R. mTORC1 activity negatively regulates human hair follicle growth and pigmentation. EMBO Rep.

2023 Jul 5;24(7):e56574. doi: 10.15252/embr.202256574. Epub 2023 May 22. PMID: 37212043; PMCID: PMC10328083.