Albinism

What is albinism?

Albinism is a genetic deficiency of melanin pigment production. Several different chromosomes are involved, depending upon the type. Albinism is usually inherited as an autosomal recessive condition but some forms are X-linked.[1]

19 genes are involved in the oculocutaneous, ocular, and syndromic (Hermansky-Pudlak Syndrome and Chediak-Higashi Syndrome) forms of albinism.[2]

Oculocutaneous albinism (OCA) affects the eyes, hair and skin, whereas only the eyes are affected in ocular albinism (OA). While most people with albinism have very light skin and hair, levels of pigmentation can vary depending on one's type of albinism. OCA involves the eyes, hair and skin. OA, which is much less common, involves only the eyes, while skin and hair may appear similar or slightly lighter than that of other family members.

How common is albinism? (Epidemiology)[3]

About 1 in 70 people carry a gene for OCA. Approximately 1 in 17,000 people in Europe and the USA have one of the types of albinism, although in some parts of the world it is more common than this. In Tanzania 1 in 1,500 live births are affected, mostly with OCA3. Albinism can affect all races and it also affects other species, including mice.

Most children with albinism are born to parents who have normal hair and eye colour for their ethnic backgrounds.

Symptoms of albinism (Presentation)[3]

Many people with albinism are diagnosed soon after birth, due to the obvious pigmentary features and developing ocular signs. However, some forms of albinism are more subtle and in fair-skinned populations a pale child with pale hair may not immediately appear to be different.

Symptoms[4]

- Visual problems are the main feature of albinism.
- Foveal hypoplasia is common to all types. Melanin is reduced or absent where it is normally present in the eye (including, crucially, the retinal pigment epithelium), skin, hair and brain. There is maldevelopment of neural pathways related to vision.
- Nystagmus, photophobia and strabismus are typical features.
- Visual acuity is almost invariably markedly reduced, with absence of binocular vision.

Signs

The precise appearance varies between types.

- The colour of the iris varies from a dull grey to blue and even brown. A brown iris is common in ethnic groups with darker pigmentation.
- Hair varies from white to yellow, reddish, grey or brown.
- There is often a reddish or violet hue reflected through the iris from the retina and the eyes appear red.
- Parents often note poor fixation on faces and objects and a delay in visual development.
- Nystagmus typically develops by 6 to 8 weeks of age and is typically pendular in nature. The amplitude diminishes as the child matures and in some cases may become latent nystagmus. Patients typically report that nystagmus becomes more noticeable with fatigue and illness.
- Some patients develop an anomalous head posture to dampen the nystagmus, referred to as the null point, where visual acuity is usually improved.

- Prism and alternate cover test often reveals strabismus.
- Iris transillumination is commonly present. The degree can vary and a grading scheme has been described, from grade 1 (marked amount of pigment) to grade 4 (absence of pigment).
- Foveal hypoplasia is usual. A few patients have some foveal development. Retinal thinning in the foveal area may be demonstrated with optical coherence tomography.

Classification[5] [6]

Oculocutaneous albinism type I (OCA1)

- This is an autosomal recessive disorder caused by mutation in the tyrosinase gene on chromosome 11. Tyrosinase is the rate-limiting enzyme in the production of melanin by melanocytes.
- People with OCA1 have no pigment in their hair, skin and eyes.
- The condition does not vary with race or age.
- OCA1 is divided into two subtypes:
    - OCA 1A with absent tyrosinase activity.
    - OCA 1B with reduced tyrosinase activity.
- About 1 in 40,000 people have some form of OCA1.

Oculocutaneous albinism type IA (OCA1A)

- Affected people have no active tyrosinase and do not make any melanin in their skin, hair or eyes.
- They are born with white hair and skin and blue eyes, although the hair may become more yellow in adulthood. The phenotype is the same in all ethnic groups around the world and at all ages.
- With time, the hair may develop a dense rather than a translucent white or a slight yellow tint.
- The iris is translucent and appears pink early in life and often turns a grey-blue colour with time.

- No pigmented lesions develop in the skin, although amelanotic naevi can be present.
- Visual acuity is so poor they are classified as severely sight impaired. Vision does not improve with age. Vision usually ranges from 20/200 to 20/400.

Oculocutaneous albinism type IB (OCA1B)

- These patients have some tyrosinase activity.
- Patients have little or no pigment present at birth but develop varying amounts of melanin in the hair and the skin in the first or second decade. This varies from very little to nearly normal skin and hair pigment.
- Ethnic and family pigment patterns influence the pigmentation.
- Sun exposure may cause some tanning of the skin but it is more common to burn.
- Near-normal cutaneous pigmentation can lead to confusion with ocular albinism and the hair can develop a golden colour ('yellow albinism'). Very few freckles develop. Eyelash pigment is often darker than that of the scalp hair.
- Visual acuity is very poor but may improve with age.

Subtypes of OCA1B

These represent different mutations:

Minimal pigment OCA (platinum OCA)

- There is white skin and hair, blue irides with no pigment at birth.
- There is an increase in iris pigment over the first decade.

Temperature-sensitive OCA1B TS

- This type of mutation of the tyrosinase gene produces an enzyme that does not work at central body temperature, as on the scalp and under the arms; however, it does work in cooler parts of the body, such as the arms and legs, to produce pigmentation in these areas.

Albinism, yellow mutant type

- This subtype of OCA1B yellow mutant type is more common among the Amish than in other populations. It results in blonde hair and the development of skin pigmentation during infancy.

Tyrosinase-positive oculocutaneous albinism (OCA type II, or OCA2)

- This is the most prevalent type of albinism in the world, primarily because of the high frequency in equatorial Africa (1:1,100 in parts of Nigeria).
- The most common type of albinism, is caused by mutation of the P gene on chromosome 15.
- People with OCA2 generally have more pigment and better vision than those with OCA1 but cannot tan like some with OCA1b. A little pigment can develop in freckles or moles.
- Solar lentigines (brown spots and freckles) can develop in sun-exposed regions of the skin but tanning is usually absent.
- People with OCA2 usually have fair skin but often not as pale as OCA1, and pale blonde to golden, strawberry blonde, or even brown hair, and most commonly blue eyes.
- Affected people of African descent usually have yellow hair, pale skin and blue, grey or hazel eyes.
- About 1 in 15,000 people have OCA2.
- OCA2 is an autosomal recessive disorder with mutation on chromosome 15.
- In Caucasian individuals the amount of pigment present at birth varies from minimal to moderate.

Oculocutaneous albinism type III (OCA3)

- It is caused by an autosomal recessive mutation in tyrosinase-related protein-1 gene on chromosome 9, leading to reduced eumelanin synthesis.
- There are 'brown OCA' and 'rufous albinism' subtypes. Cases have been reported in Africa, Puerto Rico and New Guinea.
- Affected individuals typically have red hair, reddish-brown skin and blue or grey eyes.

- The hair and skin colour are light brown; freckled skin and reddish hair may be present and the iris is grey to tan at birth.
- Affected individuals are primarily recognised as having albinism because they have all the ocular features of albinism. The iris has punctate and radial translucency and moderate retinal pigment is present.
- The skin may darken with sun exposure.

Oculocutaneous albinism type IV (OCA4)

- This is characterised by hypopigmentation of the skin and hair plus the characteristic ocular changes found in all other types of albinism, including nystagmus, reduced iris pigment with iris translucency, reduced retinal pigment, and foveal hypoplasia with reduction in visual acuity; there is misrouting of the optic nerves at the chiasm associated with alternating strabismus, reduced stereoscopic vision and an altered visual evoked potential (VEP).
- Individuals with OCA4 are usually recognised within the first year of life because of hypopigmentation of the hair and skin and the ocular features of nystagmus and strabismus. Vision is likely to be stable after early childhood.
- The amount of cutaneous pigmentation in OCA4 ranges from minimal to near normal. Newborns with OCA4 usually have some pigment in their hair, with colour ranging from silvery white to light yellow. Hair colour may darken with time but does not vary significantly from childhood to adulthood.
- Because OCA2 and OCA4 are phenotypically similar, it is not possible to accurately diagnose OCA4 based on clinical findings alone. SLC45A2 (previously called MATP and AIM1) is the only gene in which mutation is known to cause OCA4.
- OCA4 is very rare outside Japan, where it accounts for 24% of albinism cases. OCA4 can only be distinguished from OCA2 through genetic testing and is caused by mutation of the MATP gene.

Oculocutaneous albinism type V (OCA5)

- OCA5 has been found in only one family in Pakistan.

- Affected individuals have golden-coloured hair, white skin and the same visual problems that occur in OCA1. Visual acuity in this family was 6/60.
- The gene responsible for OCA5 has been located on chromosome 4 (4q24).

Oculocutaneous albinism type VI (OCA6)

- OCA6 is characterised as having golden to light to dark brown hair, white skin and brownish irides.
- OCA6 is considered an autosomal recessive ocular albinism (AROA), although individuals are hypopigmented when compared to their parents.
- Only a few individuals have been identified with this type of albinism and all of the clinical features of OCA6 have not been determined but the reduction in visual acuity is not as severe as seen in OCA1.
- OCA6 is associated with mutations in the SLC24A5 gene.

Oculocutaneous albinism type VII (OCA7)

- OCA7 is characterised with blond to dark brown hair and skin which is more hypopigmented than that of the parents.
- Individuals have nystagmus and iris transillumination.
- Visual acuity ranges from 6/18 to 3/60.
- OCA7 is associated with mutations in C10ORF11 gene on chromosome 10q22.

Ocular albinism (OA)

- OA involves the eyes only.
- Eye colour may be in the normal range but there is no pigment in the retina.
- Ocular albinism is characterised by severely impaired visual acuity and binocular vision. This does not worsen over time.
- Other associated features are nystagmus, strabismus, photophobia and abnormalities of the optic nerve pathway.

- Ocular albinism does not significantly affect the colour of the skin and hair, although the skin may be slightly fairer than that of other family members..
- There are three main subtypes.

Ocular albinism type 1 (OA1)

- This is the most common form, with a prevalence of 1 in 50,000 people; it is known as the Nettleship-Falls type, or type 1.
- The retinal pigment epithelium lacks pigment but cells elsewhere are normal.
- OA1 is an X-linked recessive ocular albinism and so affects predominantly males.
- There is usually nystagmus - OA can otherwise be difficult to detect in women, although it tends to be more obvious in men.
- There is also a red pupillary reflex (pupils appear greenish to bluish-red) with depigmented fundus and prominent choroidal vessels and photophobia.
- There is impaired visual acuity.
- Affected people have normal skin pigmentation due to foveal hypoplasia.
- Women who carry one affected chromosome have some regions of patchy pigmentation on the retina.

Ocular albinism type 2 (OA2)

- OA2 is an X-linked recessive disorder.
- It is also called Forsius-Eriksson syndrome and Åland Island eye disease, after the Åland Islands (just off the coast of Finland) where the condition was first described.
- There is foveal hypoplasia with marked visual impairment, nystagmus, myopia, and astigmatism.

- Those affected have a form of colour blindness called protanopia. This is a dichromacy - meaning that there are only two types of functional cone receptors, rather than three. Red receptors are absent, so red-green colour blindness is absolute.
- There is often night blindness.
- Female carriers may have abnormal colour vision.

Autosomal recessive ocular albinism (AROA)

- AROA is a group of genetic disorders in which reduced pigmentation of the eye is associated with decreased visual acuity, nystagmus, strabismus, and photophobia.
- Pigmentation of skin and hair is relatively normal.
- Previous studies suggest that AROA may be a mild version of OCA type I or II.[7]

Waardenburg's syndrome (WS)[8]

- WS is characterised by pigmentary and ocular features with sensorineural deafness. The most common type is inherited as an autosomal dominant genetic condition, although type 2, which is seen in association with ocular albinism, is autosomal recessive.
- Many people with WS have normal hearing but over half have profound hearing loss, usually in both ears. The hearing loss is congenital, sensorineural and non-progressive.
- People often have iris hypopigmentation, with pale blue eyes or different-coloured eyes. Sometimes one eye has segments of two different colours. Many patients have choroidal hypopigmentation.
- Nearly half of people with Waardenburg syndrome have a white forelock. Early greying of the hair is also a common feature.

There are many other rare subtypes of ocular albinism.

Diagnosis[9]

- Diagnosis is based on careful history of pigment development and an examination of the skin, hair and eyes. The only type of albinism that has white hair at birth is OCA1.
- Hair bulbs from the scalp can be used to assess tyrosinase activity. The catalytic activity of tyrosinase is determined by a radioactive biochemical assay. A negative result indicates OCA1A but a positive result still leaves the possibility of OCA1B, OCA2, OCA3, or OA1.
- Genetic testing will determine the specific type of albinism in an individual. The test is useful only for families that contain individuals with albinism and it cannot be performed practically as a screening test for the general population. Not all of the mutations that cause albinism and can be detected.
- Optical coherence tomography can be a useful adjunct in cases of OCA which display atypical features.[10]

Associated diseases

- There is an association between OCA2 and the hypopigmentation found with Prader-Willi syndrome and Angelman's syndrome. Many individuals with Prader-Willi syndrome are hypopigmented but most do not have ocular features of albinism.
- The Hermansky-Pudlak syndrome (HPS) includes OCA and the accumulation of a material called ceroid in tissues throughout the body. HPS is very rare, except in Puerto Rico where it has a prevalence of 1 in 1,800. The most important medical problems in HPS are related to interstitial lung fibrosis, granulomatous colitis and mild bleeding problems.
- The Chediak-Higashi syndrome (CHS) is a rare syndrome that includes an increased susceptibility to bacterial infections, hypopigmentation and the presence of giant granules in white blood cells. Skin, hair and eye pigment is reduced or diluted.

Albinism treatment and management[9]

Management is symptomatic, as the failed visual neural development cannot be corrected. Management aims at maximising useful vision through optometry.

Acuity correction

- Astigmatism is the most common eye problem across all the subtypes, whilst there is a high frequency of hypermetropia in OCA1A patients.[11]
- Corrected visual acuity ranges from 6/6 to 6/120, legally severely sight impaired. Near-normal vision is unusual even with glasses.
- Young children may simply need glasses and older children can sometimes benefit from bifocal glasses.
- Low vision clinics may prescribe telescopic lenses mounted on glasses, sometimes called bioptics, for close-up work as well as for distant vision. Recently, smaller and lighter telescopes have been developed. Recent advances include contact lenses with an iris tint and clear pupil area and bi-level telemicroscopes fitted to prescription spectacles.[12]

Photophobia

- Dark glasses or photochromic lenses are used for the discomfort of photophobia, although they do not appear to improve vision.

Learning adaptations

Most children with albinism can function in a mainstream classroom environment, provided the school gives specific attention to their special needs for vision. Preschool evaluations allow parents and teachers to form an Individual Education Plan for the child. Braille is unnecessary and children with albinism will read the dots visually. Various classroom aids help children with albinism:

- **High-contrast written material**: children with albinism have difficulty reading worksheets and papers that are light-contrast or low-contrast. Black on white high-contrast material is better.

- **Large-type textbooks**: the school can usually obtain large-type editions from the publishers of their regular textbooks. Because children with albinism often have difficulty keeping track of their place on the page while shifting back and forth between a textbook and a worksheet, it may help to allow them to write in the textbook. Worksheets may need to be copied on a machine that enlarges print size. Children with albinism do not always need large-type materials; however, large type should not be a substitute for optical visual aids. Use of podcasts and other aural material may be preferable to voluminous reading.
- **Copies of the teacher's board notes**: the child with low vision can read the notes close-up while classmates read the board.
- **Various optical devices**: hand-held monoculars, telescopic lenses mounted over eye glasses, video enlargement machines (closed circuit TV) and other types of magnifiers may help some people with albinism.
- **Computers**: children with albinism should begin keyboarding skills early, since computers with software for large character screen display can help greatly with writing projects.
- **Social difficulties**: children with albinism can experience particular difficulty with bullying and social relationships because their condition is particularly visible. Various strategies (eg, talking to friends, choosing one's battles, ignoring insults and attention to personal appearance) are recommended.

Sun protection

- People with albinism are very susceptible to burning and subsequent skin malignancies. High-factor sun protection cream and avoidance of sunlight are essential.[3]

Nystagmus

- For nystagmus, eye muscle surgery can reduce the movement of the eyes. However, vision may not improve.
- People with albinism may find ways of reducing nystagmus while reading, such as placing a finger by the eye, or tilting the head at an angle where nystagmus is dampened.

Strabismus

- Ophthalmologists prefer to start treatment when patients are about 6 months of age, before the function of their eyes has developed fully.
- They may recommend a patch over one eye to promote the use of the non-preferred eye. In other cases, the alignment of the eyes improves with the wearing of glasses.
- Correction of strabismus by surgery or by injection into the extraocular muscles does not completely correct the problem with both eyes fixing on one point.
- Improving the alignment of the eyes enhances psychosocial development and interpersonal interactions but also cannot correct the improper routing of the neural pathways.
- Depth perception is not improved with eye muscle surgery.

Complications of albinism

Protection from the sun is essential to prevent burning and cutaneous malignancies, including basal cell carcinoma, squamous cell carcinoma and malignant melanoma. This is particularly important in Africa (or other places where the sun is very strong) but should not be forgotten in temperate climates. Otherwise, life expectancy is normal. Albinism may cause social problems because people with albinism look different from their families, peers and other members of their ethnic group.

Skin problems

People with albinism are very susceptible to burning and subsequent skin cancers. High-factor sun protection cream (20 SPF or higher) and avoidance of sunlight are essential. In practical terms this may be difficult in countries where there is no market for strong sun protection as most of the population do not need it.

Social difficulties

- Children with albinism may experience difficulty with bullying and social relationships because their condition is visible. In some ethnic groups the difference is dramatic and stigmatising, and the racial identity or paternity of the child may be questioned.

- People with albinism have been subject to negative portrayal in film, with an emphasis on strangeness as well as villainy.
- In China albinism is considered bad luck, leaving people with albinism ostracised and excluded from mainstream society. Chances of schooling, job prospects and marriage are often limited.
- Persecution of people with albinism is based on the belief that certain body parts of people with albinism can transmit magical powers and this is particularly problematic in Tanzania and Malawi. In sub-Saharan East Africa, people with albinism have been ostracised and even killed because they are presumed to be cursed and bring bad luck.[13]

Prognosis

Growth, development and intellectual development in the child are normal. Vision is invariably severely impaired.[3]

A spectrum of structure and function exists in albinism. Better vision is achieved in those without nystagmus, with measurable stereopsis, with some melanin pigment in the macula and with a rudimentary annular reflex in the macula. As research progresses, other methods of improving visual acuity in children and adults may emerge.[5]

Prevention[3] [14]

Carrier detection and prenatal diagnosis are possible if the relevant genetic mutations have been identified in the family. Amniocentesis is performed at 16-18 weeks of gestation.

However, given proper support, children with albinism can function well, despite considerable visual handicap, and have a normal lifespan, so not all affected families will want this.

Dr Mary Lowth is an author or the original author of this leaflet.

Further reading

- Albinism fellowship

- National Organisation for Albinism and Hypopigmentation
- Mondal M, Sengupta M, Samanta S, et al; Molecular basis of albinism in India: Evaluation of seven potential candidate genes and some new findings. Gene. 2012 Dec 15;511(2):470-4. doi: 10.1016/j.gene.2012.09.012. Epub 2012 Sep 23.

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