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Alkaptonuria and ochronosis

What is alkaptonuria and ochronosis?

Alkaptonuria is a rare genetic disease that is characterised by passing urine that becomes black when left standing. The earliest sign of the condition is usually dark staining found in nappies or diapers of infants.

The most obvious sign in adults is a thickening and blue-black discolouration of the ear cartilage. This blue-black discolouration of connective tissue (including bone, cartilage, and skin) is caused by deposits of yellow or ochre-coloured pigment is called ochronosis.

What causes alkaptonuria and ochronosis?

Alkaptonuria is an autosomal recessive inherited disorder, which means that two abnormal genes (one from each parent) are needed to have the disease. The defect causes the body not to produce enough of an enzyme called homogentisic acid oxidase. This enzyme normally breaks down a toxic by-product of tyrosine metabolism called homogentisic acid. Although some of this is excreted in urine, small amounts remain in the body and slowly and progressively get deposited in bones and cartilage where it turns into a pigmented polymeric material.

Ochronosis may also be caused by external agents. These may include:

- Medications such as quinacrine and quinine
- Deposits of phenol (carboxylic acid), used in the past to treat [leg ulcers](#)
- Excessive use of [hydroquinone](#) (in this case, cartilage is not affected).

What are the clinical features of alkaptonuria and ochronosis?

Most patients don't have any symptoms throughout childhood or early adult life and it is not until they reach their 40's that other signs of the disease start appearing. One of the earliest signs is thickening of the ear cartilage (the pinna feels noticeably thickened and flexible). In addition the skin turns a blue-black colour. Earwax is often reddish-brown or jet-black. Gradually patients will suffer sore joints, leading to arthropathy (joint disease characterised by swelling and enlarged bones). Many body parts become affected due to the build-up of pigment deposits in bones and cartilage.

- Bones and cartilage of the lower back, knees, shoulders and hips are most affected. Firstly patients suffer low back pain with stiffness, followed by knee, shoulder and hip pain over the next 10 years. Cartilage becomes brittle and can break apart easily. In some cases this leads to spinal injuries such as prolapsed intervertebral discs.
- Deposits around the trachea (windpipe), larynx (voice box) and bronchi (air passages to the lungs) may cause shortness of breath and difficulty breathing.
- Deposits around the heart and blood vessels can calcify (harden) and lead to atherosclerotic plaques (hard spots in arteries).
- Pigmentation of the sclera of the eye usually occurs early on. This does not affect vision but appears as brown or grey deposits on the surface of the eye.
- Skin colour changes are most apparent on areas exposed to the sun and where sweat glands are found. Areas most affected include the cheeks, forehead, armpits and genital regions. The skin takes on a blue-black speckled discolouration. Sweat produced has been found to stain clothes. Sometimes nails can be

affected and turn a distinct brown colour.

What is the treatment for alkaptonuria?

Alkaptonuria is a lifelong disease. There is no cure for the condition. If alkaptonuria is diagnosed early on in life it is reasonable for patients to have a low-protein diet. This reduces the intake of amino acids phenylalanine and tyrosine, which in turn reduces the amount of homogentisic acid produced. Although not proven, this could potentially avoid or minimise complications later in life.

Vitamin C has been found to slow down the conversion of homogentisic acid to the polymeric deposits in cartilage and bone. A dose of up to 1g/day is recommended for older children and adults. Nitisinone, an enzyme inhibitor that mediates the formation of homogentisic acid is being used in restricted experimental treatments.

Life expectancy is normal although patients may be at increased risk of heart conditions and may require surgical treatments for spine, hip, knee and shoulder joint problems.

Exogenous cutaneous ochronosis has been successfully treated by [laser](#).

Related information

- Book: Textbook of Dermatology. Ed Rook A, Wilkinson DS, Ebling FJB, Champion RH, Burton JL. Fourth edition. Blackwell Scientific Publications.

References:

On DermNet NZ:

Other websites:

- [Alkaptonuria](#) - emedicine, the online textbook
- [Alkaptonuria Society](#)

Books about skin diseases:

See the [DermNet NZ bookstore](#)

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DermNet does not provide an on-line consultation service.

If you have any concerns with your skin or its treatment, see a [dermatologist](#) for advice.

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