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UNDERSTANDING GENES & CHROMOSOMES

Cockayne syndrome

rarechromo.org

This guide is designed to help families and healthcare professionals looking after people with Cockayne syndrome. It contains information about the cause, the ways in which it can affect people and suggestions about the help and management that can benefit people with this condition.

What is Cockayne syndrome?

Cockayne syndrome (CS) is a rare genetic condition associated with premature ageing, growth failure, developmental delay, varying degrees of learning (intellectual) disability and behavioural differences. It has a spectrum of features that are split into four main subtypes according to the age at which features become apparent and how severe they are:

- **COFS** – (Cerebrooculofacioskeletal syndrome) is the most severe form, features are identified before birth
- **CSI** – is the most common form, features become apparent in the first two years of life and are severe
- **CSII** – is a severe, early onset form and features are present at birth
- **CSIII** – is a milder, later-onset form and features become apparent in childhood or adolescence

There are also currently discussions regarding the possibility of a late onset CS type iiii that might effect adults, but as yet (2026) this has not been reported in the published literature. (Amy and Friends, private communication 2026).

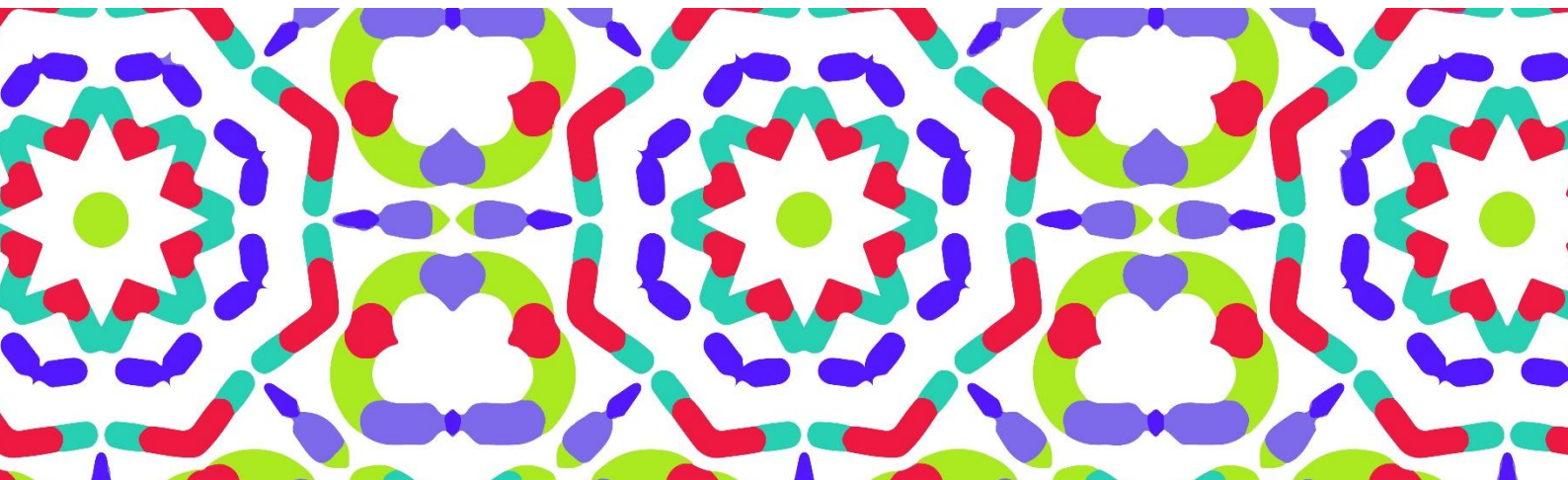
As is common with genetic conditions, each person can be affected differently - even among affected members within the same family. Not everyone with Cockayne syndrome will have all the possible features and each person with a certain feature won't necessarily be affected by it to the same level as other people with that feature.

Cockayne syndrome is caused by changes (variants) in the ERCC8 gene (also known as CSA) or the ERCC6 gene (also known as CSB), with changes in ERCC6 being more common. Deletions of the genes, or parts of the genes can also cause Cockayne syndrome but are less common.

How common is Cockayne syndrome?

Cockayne syndrome is extremely rare. The estimated incidence in Western Europe is approximately 2.7 babies per million births but only a few hundred people have been reported in the medical literature.

While Cockayne syndrome affects people worldwide, its frequency can be higher in specific, often isolated, communities due to a founder effect (as explained later in the 'What causes Cockayne syndrome section').



What features and symptoms do people with Cockayne syndrome have?

As is common with many genetic conditions, children and adults with Cockayne syndrome can have a range of features and symptoms. As more people are diagnosed, and information is shared, the range of features, and the likelihood of a child or adult having these features, will become clearer.

Common features

Most people with Cockayne syndrome have:

- Growth failure and an unusually small head (microcephaly); while head circumference is typically standard at birth, its growth slows and often stops between one and two years of age
- Anomalies on brain imaging
- Low muscle tone (hypotonia)
- Joint contractures
- Hearing loss, which affects most people and is almost always in both ears (bilateral)
- Tremor
- Sensitivity to sunlight (clinical photosensitivity)
- Gastro-oesophageal reflux
- Problems with nutritional intake, commonly reported and often requiring feeding support
- Sideways curvature of the spine (scoliosis)
- Cataracts
- Developmental delay and intellectual disability
- A distinctive facial appearance that develops over time, characterised by sunken eyes, a prominent or sharp nose, a jutting chin and thin lips
- Other common neurological issues such as coordination difficulties (cerebellar ataxia), stiff muscles (spasticity) and nerve damage outside of the brain and central nervous system (peripheral neuropathy)
- Other common vision or eye anomalies such as degeneration of the retina (retinal dystrophy) or optic nerve (optic atrophy) and light sensitivity (photophobia)

Other possible features include:

- Dental anomalies, such as a high rate of dental caries (tooth decay), which may be due to low amounts of tooth enamel (enamel hypoplasia) and saliva
- Thinning hair, noted in almost half of individuals in one study
- Seizures
- Respiratory problems
- Darker patches of skin (kin hyperpigmentation)
- Antenatal ultrasound anomalies, most commonly as prenatal growth restriction
- Other skeletal anomalies including low bone density (osteopenia) and forward curvature of the spine (kyphosis)

It is important to note that, unlike other DNA repair disorders, there is no increased risk of skin cancer.

He was my biggest blessing and my greatest accomplishment.”

Pregnancy and birth

While most pregnancies are unremarkable and proceed without complication, some concerns during pregnancy have been reported, sometimes following mid-pregnancy anomaly scans. In one study of 87 pregnancies, anomalies were detected on 21 scans (Wilson 2016). Where a cause for concern was noted, most often parents reported slow growth in the womb (intrauterine growth retardation IUGR). Other anomalies reported include joint contractures (arthrogryposis) and unusually small eyes (microphthalmia).

Some babies show some signs of difficulty at birth, related to difficulties with feeding. Other issues can include hearing loss, congenital cataracts (in severe forms), poor peripheral circulation causing cold hands and feet, and particularly difficult nappy/diaper/pad rash (depending on age). Birth weights are usually below average. A small number of babies grow very slowly in the womb and are tiny at birth. In one study (Wilson 2016) it was noted that roughly one third of deliveries were Caesarean deliveries. Children with the most severe form of Cockayne syndrome (CS type II) show little or no neurological development after birth; sadly, these children often pass away before the age of five.

Appearance

Certain facial features are found more often in children with Cockayne syndrome than in other children. These features may mean that you see unexpected similarities between your child and others with Cockayne syndrome. These features develop over time and become more pronounced due to a loss of fat under the skin, which can create a thin, aged appearance. The most common characteristic features include a small head (microcephaly); deep-set eyes (enophthalmos); a sharp, thin, or beaked nose; a jutting chin (prognathism); large, sometimes malformed ears; and thin lips.

Other characteristics can include a small stature with disproportionately long limbs, a stooped posture, and skin that is very sensitive to sunlight (photosensitivity). Dental anomalies, such as tooth decay and missing or delayed teeth, are also common.

Development

Gross and fine motor skills

Progressive developmental delay affecting gross and fine motor skills has been reported in all children with Cockayne syndrome. The degree of delay ranges from mild to profound. In adults with Cockayne syndrome type III, a characteristic triad of motor issues that begins in childhood is seen, which includes muscle stiffness (spasticity), difficulties with coordination (ataxia) and nerve damage (peripheral neuropathy).

A number of motor-related issues are common and may affect mobility, including:

- High muscle tone (hypertonia) and dystonia (involuntary muscle contractions)
- Spasticity (stiffness)
- Peripheral neuropathy (damage to peripheral nerves)
- Muscle weakness and muscle atrophy (loss of muscle mass)
- Tremor
- Variable reflexes, which can be overactive (hyperreflexia) or underactive (hyporeflexia)

Some children may have an unusual gait when walking because of stiffness or balance issues (known as ataxia) and may also have a characteristic stooped posture. In those with Cockayne syndrome type I, ataxia, tremor, and an unusual gait or inability to walk are seen in 10% or more of individuals. For some, independent walking may not be achieved.

These motor difficulties have a significant impact on daily living. Fine motor difficulties can make activities like feeding, grooming, dressing and writing difficult. Oral motor difficulties can cause choking, gagging, or poor feeding coordination, sometimes requiring feeding support (such as a nasogastric or gastrostomy tube). There is also a risk for later-onset orthopaedic complications, including joint contractures, scoliosis (curvature of the spine) and hip dislocation.

Many children benefit from early intervention and medical equipment such as wheelchairs, walkers, adaptive strollers and orthotics.

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He is stronger than he looks."

Intellectual development and learning

Most children with Cockayne syndrome have learning (intellectual) disability (LD/ID) or learning difficulties. This often involves developmental regression, where skills and abilities decline over time. LD/ID ranges from mild to profound but is usually in the severe range. The onset and rate of cognitive progression are variable depending on the type of Cockayne syndrome. In CS type I, development typically slows within the first two years of life, followed by progressive decline. In the infantile subtype (CS type II), there may be little or no brain development after birth. However, very rare exceptions have been reported, including individuals with milder forms of the condition who have standard intelligence. Most children will require significant additional support with their learning throughout their education. Despite the cognitive challenges, sociability may be an area of relative strength.

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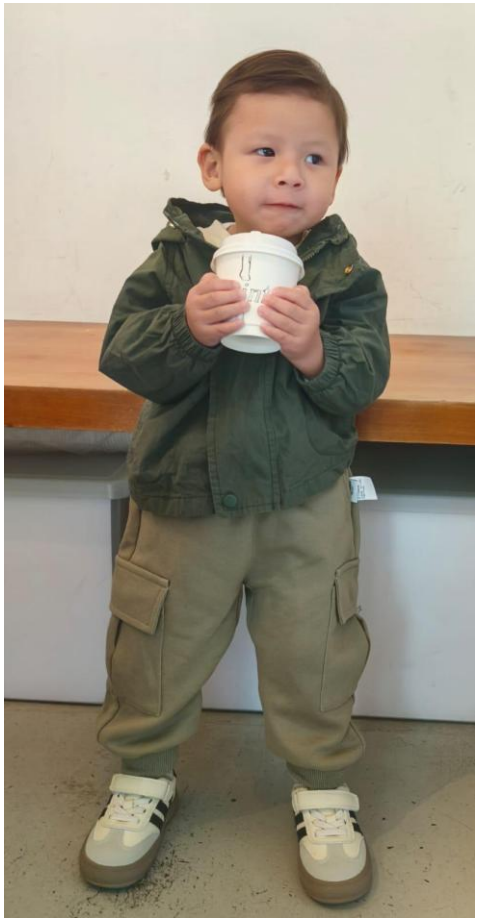

I was diagnosed with CSB - type 2 at the age of 3.5 (2026). I love going to school, and spending the evening and night with my supportive and loving family, especially my elder brother who loves me wholeheartedly. I don't personally like going to physio session, I cried and puked every time, but I still carry on because I want to hang in there till the CSB gene therapy is going alive. I live my life like all other kids in the world, though I couldn't stand or walk on my own, and couldn't verbally express myself. I do communicate well with my family using our own self-created sign language. I am very positive and happy, I am fighting hard every day against the disease. Please help spread the word to make this ultra rare disease not so rare."

Speech and language

Children with Cockayne syndrome typically experience some degree of speech and language delay. These challenges often become evident within the first two years of life, and early signs in infants may include a weak cry and poor feeding. The eventual range of achievement is broad, but some may remain non-verbal (affected or absent speech occurs in

10% or more of individuals with CS type I). Those who do develop speech may achieve single words (and may have difficulties with articulation), short phrases or simple sentences. A common observation is that a child's understanding of language (receptive language) is significantly better than their ability to speak (expressive language), although receptive abilities can also be affected. These difficulties are caused by the progressive deterioration of central and peripheral nervous system function and are often made more challenging by progressive problems with vision and hearing.

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"When our daughter was born she reached all of her milestones until about the age 2. I noticed that she wasn't talking much, so I talked to the pediatrician about it. He just shrugged it off as being a second child. I went 2 years trying get him to listen to me about my concerns before I told him to just send us a specialist. Once we saw the specialist, we started to get answers, but not the correct answers. It took us 6 years and 4 genetic tests before we got her official Cockayne syndrome diagnosis."

Feeding

Feeding difficulties and gastrointestinal complications are significant clinical concerns in Cockayne syndrome, affecting nutrition and overall health. Feeding issues in the new-born period are common. These challenges are often due to issues with muscle control in the mouth and throat (oral motor dysfunction), which can lead to choking, gagging, difficulties with swallowing and refusing to feed. Difficulties with fine motor skills can also make self-feeding more challenging. Many babies also suffer from gastro-oesophageal reflux (GERD/GORD) (in which feeds return readily up the food passage), with studies reporting this in between a third and a half of individuals (Wilson 2016). The functional impact of these feeding difficulties is significant, frequently leading to poor weight gain and frequent chest infections (due to aspiration). Over time, these difficulties can contribute to severe growth failure, a loss of body fat, and a severe and progressive wasting syndrome known as cachexia. This often becomes clear by the time a child reaches preschool age.

Even with intensive support, feeding is often described as "always difficult", and children may struggle to gain weight.

Unique publishes a separate guide to Feeding

"At four months old, we heard the words Cockayne syndrome — words that changed our lives forever. Our son entered this world fighting before he could even cry. From birth battles to a G-tube journey, he has proven he is more than a diagnosis, more than tubes and hospital rooms. He is strength in its purest form — a tiny warrior teaching us how powerful love, resilience, and hope can truly be. Never defined by his condition, he continues to show us what true courage looks like every single day."

Growth and stature

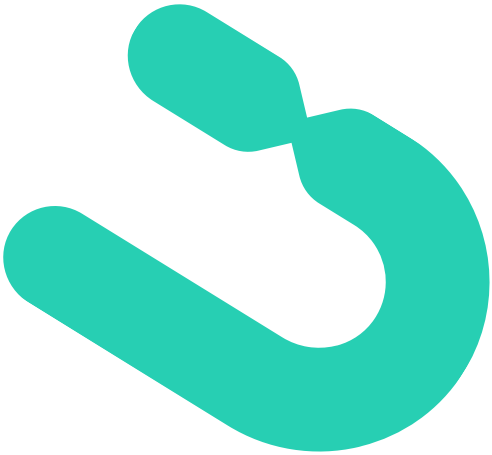
All children with Cockayne syndrome described in the medical literature so far (2026) are noted as having growth delay and short stature (Wilson 2016). The age when this begins can vary and depends on the specific subtype of the condition. While prenatal growth and birth measurements are typically within the expected range, growth failure becomes evident within the first two years for CS type I, is present at birth for CS type II, and begins after two years of age for CS type III. Many children also have a smaller than expected head size (microcephaly), though head circumference at birth is usually within the standard range. Beyond infancy, height and weight remains below average. The degree of short stature in adults can be variable, with one

study noting extreme short stature (height less than 135 cm) in just under three quarter of those reported (Rapin 2006). Progressive and severe weight loss (cachexia) is also a common feature that can become obvious in the preschool years.

Behaviour

Behavioural anomalies are a recognised neurological feature in Cockayne syndrome, occurring in 10% or more of individuals with CS type I (Laugel 2000). The syndrome is characterised by progressive behavioural deterioration that occurs alongside intellectual decline. Children with Cockayne syndrome typically tend to have behaviour in keeping with their overall degree of developmental delay, and most have a happy disposition (sociability is often unaffected and individuals can retain an outgoing personality, with one report noting this was the case even while the person was experiencing advanced dementia and cachexia (Rapin 2006). Understanding this complex profile is key to providing effective support.

Unique publishes a separate guide to Challenging Behaviour



“Our son, lovingly known to everyone as "Baby," had a smile that could light up any room. He was truly an angel on this earth, and his presence radiated a pure and unconditional love that everyone around him could feel. He was our greatest blessing. In 2013, Baby was diagnosed with Cockayne syndrome Type II (ERCC6). Through the many challenges he faced, he had an incredible ability to recognize and remember people. He expressed his love and connection through the way he looked at you and the sweet, coy smirk that could instantly melt your heart. Baby taught each of us a profound lesson: although his body and health had limitations, his love, spirit, and personality knew no bounds. He touched countless lives with his strength, resilience, and joy.”

Puberty

There is limited information available about puberty in children with Cockayne syndrome. For some, it may incomplete or atypical. In boys, this can include underdeveloped testes and a small phallus (seen in almost one-third of individuals (Rapin 2006). In girls, breasts are often underdeveloped. The UK based charity Amy and friends have shared that many of the children they support reach puberty within the standard age range and some have experience early puberty (Amy and Friends, private communication 2026). The impact on menstruation is variable; one girl was reported to have had regular periods, and another woman with Cockayne syndrome had a successful pregnancy. Some families of children with genetic disorders and behavioural or learning difficulties can be particularly concerned at their daughter’s ability to cope with menstruation, and for some discussing menstrual regulation options with a paediatrician may be beneficial.

Unique publishes a separate guide to Puberty

Adulthood

Survival into adulthood in Cockayne syndrome (CS) is exceptional, with most individuals sadly passing away in childhood. For those who survive longer, the condition involves a progressive and multisystemic decline, and there is currently no curative treatment.

Experiences of adulthood are likely to vary considerably and will depend on many factors. These include the level of any learning disability/intellectual disability (LD/ID) and possible on-going medical concerns. Premature ageing is a key feature of CS, characterised by the degeneration of multiple tissues and a progressive loss of the skills needed for independent living. This often follows a predictable pattern, with the characteristic ‘aged’ facial appearance typically appearing in adolescence.

Adults with Cockayne syndrome have varying levels of independence, which is affected by motor issues and joint contractures. A few individuals with milder forms of CS have gone on to have families of their own. Most adults continue to live with their parents or in supported settings such as a group or residential care home, with caregivers who can provide support.

The condition is associated with a progressive decline in neurological and cognitive function. This can include:

- Muscle tightness (spasticity)
- Difficulties with coordination, balance and speech (ataxia)
- Nerve damage (peripheral neuropathy)
- A progressive loss of learning capacity, which can develop into dementia, typically in a person's twenties

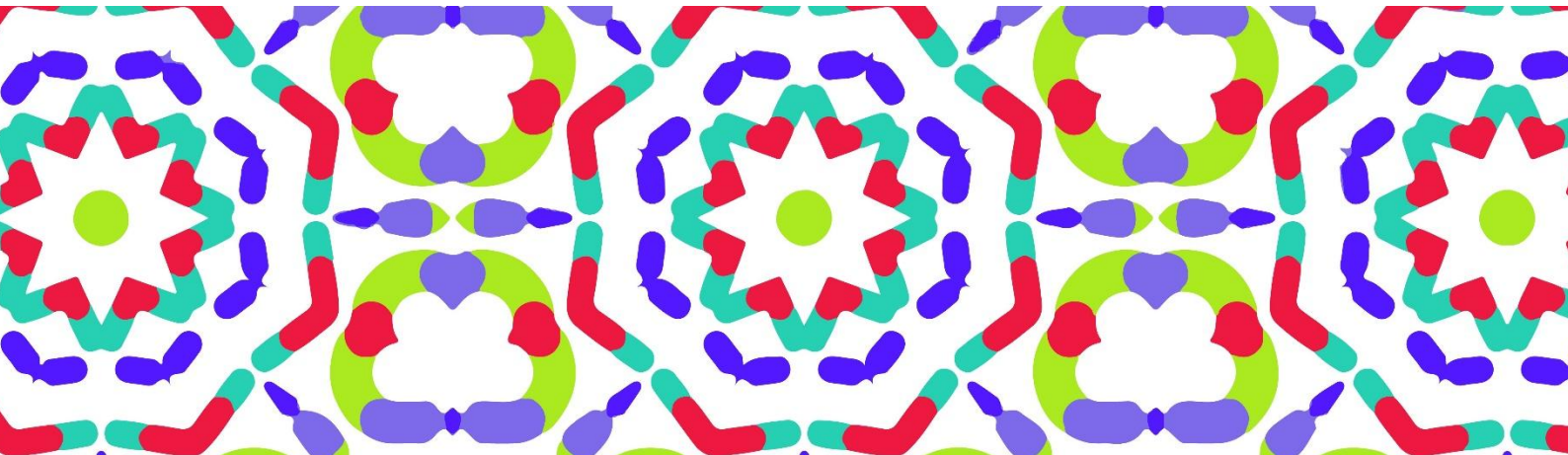
Despite this profound neurological decline, a striking feature is that many individuals have a preserved and outgoing personality.

Adults with CS require ongoing health checks for numerous complications affecting the whole body. These can include:

- Vascular and kidney issues, such as early narrowing of the arteries (atherosclerosis), high blood pressure (hypertension) and kidney failure
- Endocrine problems, such as type 2 diabetes and hormone-related issues (hypogonadism)
- Skeletal problems, including low bone density (osteopenia), joint contractures and curvature of the spine (kyphosis and scoliosis)

Unique publishes a separate guide to Transition

Live every day to the fullest and be thankful for each moment. Avoid comparing your child to others—although they may have similarities, every child follows their own unique journey.”



Medical concerns

The following medical concerns have been found in children with Cockayne syndrome. They are not found in all children so not all children with Cockayne syndrome will be affected.

Heart and circulation

Heart conditions that are present at birth (congenital) are not considered a characteristic feature of Cockayne syndrome. Instead, the main concerns are related to the blood vessels (vascular) and tend to develop later in life.

These can include:

- Hardening and narrowing of the main artery of the body (aortic atherosclerosis), which has been seen in several individuals, including one as young as 14 years (Rapin 2006)
- Weakening of part of the aorta (thoracic aneurysm) (Wilson 2006)

Limited information on long-term outcomes suggests these conditions can be significant.

Brain

Most children with Cockayne syndrome have a structural brain anomaly, which can be detected by MRI (magnetic resonance imaging) or a CT (computerised tomography) scan of their brain. In one study, this was seen in 71 out of 85 people (83.5%) (Wilson 2016), in this study, other changes identified included:

- Build-up of calcium in the brain (intracranial calcification), seen in 47 out of 85 individuals (55%). This most commonly affects an area of the brain called the basal ganglia
- Changes to the protective covering (myelin) of nerve fibres in the brain (white matter), such as unusual development (dysmyelination) or reduced amounts (hypomyelination), seen in 33 out of 85 individuals (38%)
- Underdevelopment (hypoplasia) of the white matter connecting the two halves of the brain (corpus callosum)
- A build-up of fluid within the brain (hydrocephaly)
- Reduction in brain volume (cerebral and cerebellar atrophy)
- Enlarged fluid-filled cavities (ventricles) in the brain (ventriculomegaly)

Seizures

Rarely children with Cockayne syndrome experience some form of seizure (a sudden and unexpected change in the electrical activity in the brain). Estimates of how many people are affected vary between studies, with one review of 140 people reporting epilepsy in 5% to 10% of individuals (Rapin 2006), while another study identified seizure disorders in 23% of individuals (Wilson 2016). Depending on the part(s) of the brain affected, symptoms vary, but include temporary confusion, uncontrollable jerking movements and loss of consciousness or awareness. Age of onset can vary considerably, while seizures may be isolated to a single incident or occur more regularly. For the majority of affected individuals, seizures are described as ongoing and can be difficult to manage. More than one type of seizure may be present in the same individual. No single predominant seizure type has been observed. Status epilepticus (a seizure that lasts for a long time) is a known risk.

Movement Disorders

Most individuals with Cockayne syndrome have a movement disorder, with motor skills being universally and progressively impaired, leading to severe disability. These movement disorders can be highly variable in frequency, duration and type and are

often seen as involuntary movements and/or spasms in parts of their bodies and may be sudden and repetitive.

All adults with Cockayne syndrome type III have a characteristic triad of motor issues that begins in childhood, including spasticity, ataxia, and peripheral neuropathy.

The movement disorders reported have included:

- Involuntary muscle movements and twisting or tightening in altered postures (dystonia)
- Stiff or rigid muscles (spasticity)
- Difficulties with coordination and balance (ataxia) which can cause an unusual way of walking (gait) or an inability to walk. In Cockayne syndrome type I, ataxia and shaking (tremor) occur in some individuals
- Shaking (tremor)
- High muscle tone (hypertonia)
- Muscle weakness (hypotonia)

Individuals may also present with a characteristic stooped standing posture. These motor impairments have a significant functional impact on daily life. Difficulties with balance and coordination affect mobility, and many individuals require support such as from wheelchairs, walking aids or orthotics. Over time, there is a risk of orthopaedic complications including joint contractures, curvature of the spine (scoliosis) and hip dislocation.

Hormones

Children with Cockayne may have conditions that affect their hormones. The most frequently reported anomalies involve gonadal function (sexual development), glucose metabolism and growth. Underdeveloped sexual characteristics (hypogonadism) is a common disturbance. In males, this can present as underdeveloped testes and a small phallus, while in adolescent and adult females, breasts are often underdeveloped.

An increased prevalence of diabetes mellitus, similar to type 2 diabetes, is also well-documented (Rapin 2000), with one study finding that 6 people out of 47 tested (13%) had abnormal glucose metabolism (Wilson 2016). This is not thought to be caused by autoimmune function.

Other conditions include an underactive thyroid (hypothyroidism), which was identified in eight individuals in one group of people (Wilson 2016), and variable growth hormone levels, which may be decreased, as expected or elevated (Rapin 2006). Severe growth failure leading to short stature is a typical feature affecting almost three quarter of adults reported in one study (Rapin 2006), but its cause, in relation to a hormone imbalance, is not clearly understood.

Ears and Hearing

Almost all children with Cockayne syndrome have a progressive hearing impairment and typically affects both ears (bilateral). Hearing loss was present from birth in 14 out of 68 babies (21%) in one study (Wilson 2016), but its onset is progressive, with 84% of individuals affected by ten years of age. For some, hearing loss may be the first symptom of the condition. This deterioration can lead to poor speech comprehension.

A hearing loss may be conductive, where sound is unable to travel effectively to the inner ear; sensorineural, where there are problems with the inner ear, sometimes with the cochlea or auditory nerve (the nerve that sends signals to the brain about sound); or a combination of both (mixed hearing loss). While a progressive,

high-tone sensorineural loss is most common, conductive or mixed hearing loss was identified in 20 individuals in one study (2016).

Unique publishes a separate guide to Hearing

Eyes and sight

Eye and vision anomalies are common in children with Cockayne syndrome. The most common issues are the development of cloudy patches in the lens of the eye (cataracts) and sensitivity to light (photophobia). Degeneration of the retina (pigmentary retinopathy) and damage to the optic nerve (optic atrophy) are also frequent findings. Vision problems in Cockayne syndrome are progressive, meaning they worsen over time and can lead to severe visual impairment.

A thorough evaluation by a paediatric ophthalmologist is recommended at diagnosis. In the most severe form of the condition (CS type II), cataracts may be present from birth.

Known concerns include long-sightedness (hyperopia); a squint, where one or both eyes turn inward, outward, up, or down (strabismus); uncontrolled repetitive eye movements (nystagmus); structurally small eyes (microphthalmia); a sunken appearance of the eyes (enophthalmos) and anomalies of the cornea, such as clouding, due to reduced tear production.

Breathing

Babies and children with rare chromosome and gene disorders tend to have a higher rate of respiratory concerns, although the presentation can be variable. One study reported 20 people out of 102 (20%) as having respiratory concerns (Wilson 2016) with respiratory infections being the most common condition affecting 15 individuals. The primary cause for these recurrent infections is thought to be aspiration (the entry of food or liquid into the airway), and the risk can be increased by later-onset complications such as a curved spine (scoliosis) and high muscle tone (hypertonia) or dystonia. Other reported issues include restrictive lung disease and asthma. In addition, other breathing anomalies have been observed, such as mixed breathing (breathing through the mouth and nose at the same time).

Hands and feet

Children with Cockayne syndrome occasionally have anomalies of the hands and feet. Most common among these are ‘claw foot’ (pes cavus), stiff or ‘frozen’ joints (joint contractures) and curved joints present from birth (arthrogryposis), particularly in severe, congenital forms of the condition.

Spine

Some babies are born with or develop a spinal curvature, either a sideways curve of the spine (scoliosis), a rounding of the upper back (kyphosis) or kyphoscoliosis (a combination of kyphosis and scoliosis). These spinal issues contribute to a stooped posture, which is a key feature of the premature ageing seen in the condition. In one study, scoliosis was reported in almost half of individuals (Wilson 2016), and for almost half of those people, the condition was progressive. The spinal changes can lead to a stooped standing posture and an unusual way of walking (abnormal gait), or in some cases, a complete inability to walk. To help with mobility, individuals may need to use equipment like walkers or wheelchairs. Individuals with the more severe CS type II may also present with stiffness of the joints and spine.

Joints

Joint anomalies are a known feature of Cockayne syndrome and tend to worsen over time. In many cases, joints are unusually tight (contractures), affecting about a third of participants in a study from the Cockayne syndrome Natural History (CoSyNH) group. These contractures affect the lower limbs more often than the upper limbs and are linked to increasing spasticity (muscle tightness). They can be severe enough to complicate daily care and can have a significant functional impact, contributing to an unsteady walk (gait instability) or a complete inability to walk. These may require surgery and tendon lengthening to extend their range of movement. Some children experience hip dislocation and this may be apparent at birth or develop later in life. One study reported that about a quarter of contractures were present from birth (Wilson 2016). In severe cases, congenital joint contractures (arthrogryposis) can occur. Contractures are treated with splinting and, if necessary, immobilisation in plaster and possibly surgery.

> ***"Hip displasia is really common among the children/young people we support - hip joints are unstable and sockets are sometimes worn or shallow but not always dislocating." Amy and Friends, private communication 2026***

Skin

The most common skin feature in individuals with Cockayne syndrome is photosensitivity (an increased sensitivity to sunlight). This can be very noticeable and may first appear in infancy, for example as a severe sunburn after minimal sun exposure. In some children, this can cause blistering (bullae) and peeling (desquamation) of the skin. Because of this, diligent, lifelong management of sun exposure is very important.

Other common skin characteristics have been identified from a study of 16 adults with Cockayne syndrome. These include:

- Dry skin
- Anhydrotic skin (a reduced ability to sweat)
- Freckles
- Pigmented skin (areas of darker skin)
- Scaly skin in sun-exposed areas

It is important to note that, unlike some other conditions with photosensitivity, individuals with Cockayne syndrome (types I, II, and III) do not have an increased risk of developing skin cancer.

Teeth

Dental concerns are very common in individuals with Cockayne syndrome, with all 14 people in one study having at least one type of dental anomaly (Bloch-Zupan 2013) and just under half of individuals in another (Wilson 2016). A number of issues have been described including unusual dental development, with variations in tooth number (hypodontia), size (microdontia) and shape (e.g. taurodontism). An unusual jaw size (micrognathia), leading to overcrowding, misalignment (malocclusion) and a deep bite has also been reported. Unusually thin, weak enamel (enamel hypoplasia) may be common, reported in 16 out of 17 individuals in one study (Bloch-Zupan 2013). Tooth grinding (bruxism) was also reported in 3 out of 17 individuals, which can prematurely wear down the enamel. Teeth may emerge late, although early eruption has also been recorded. A high standard of dental care is important as the enamel defects lead to a high susceptibility to severe dental decay (caries). Oral hygiene can be difficult and assisted brushing may be required. Gingivitis (inflammation of the gums) is also common, seen in seven out of 14 people in one study (Wilson 2016). Children and adults may also benefit from specialist hospital dental services and may require treatment under general anaesthetic,

especially as access to standard dental care can be a barrier (in one study, six out of 17 individuals had never visited a dentist (Bloch-Zupan 2013)).

Unique publishes separate guides to Looking after your child's teeth and Teeth: common concerns

Kidney and urinary tract

Some individuals with Cockayne syndrome are born with anomalies of the kidneys and/or urinary tract (seen in 4 out of 37 people in one study)(Wilson 2016). Conditions that have been described include:

- Under-sized kidneys (hypoplastic kidney)
- Abnormal kidney shape
- Kidney stones (renal calculi)

In addition to structural anomalies, functional kidney problems can also occur. High blood pressure (hypertension) has been reported in some individuals (affecting 12 out of 67 people (18%) in one study (Wilson 2016)). There have also been reports of high blood pressure leading to kidney failure (hypertensive renal failure) in adults, and a child who developed a condition causing the kidneys to leak large amounts of protein into the urine (nephrotic syndrome).

Genitals

Minor anomalies of the genitals in boys have been reported frequently (in almost one third of individuals (Rapin 2006). Most common among these are a very small penis (micropenis) and underdeveloped, wasting (atrophic), or small testes. It is not known if these anomalies affect the ability to have children.

Conditions that have been reported commonly include under-developed internal genitalia (such as atrophic ovaries and infantile sexual development) and underdeveloped or small breasts (often with relatively large nipples). Despite these findings, successful pregnancies have been reported. Some women with Cockayne syndrome are also able to menstruate. Individuals with the milder form of the condition (CS type III) may have typical reproductive capacity.

Cancer and Tumors

Individuals with Cockayne syndrome (CS), including Types I, II, and III, as well as the related Cerebro-oculo-facio-skeletal (COFS) syndrome, do not exhibit a predisposition to skin cancer or other malignancies (Laugel 2000). Other DNA repair disorders, such as xeroderma pigmentosum (XP), do have an increased risk of cancer (Rapin 2006). The low prevalence of tumours in Cockayne syndrome is supported by clinical data; a review of 16 adults with Cockayne syndrome reported no malignancies, and other summaries have not listed tumours as a clinical feature of this syndrome (Calmels 2018). It is thought that this could be explained by the increased cell death observed in this condition, preventing possible cancer cells from multiplying.

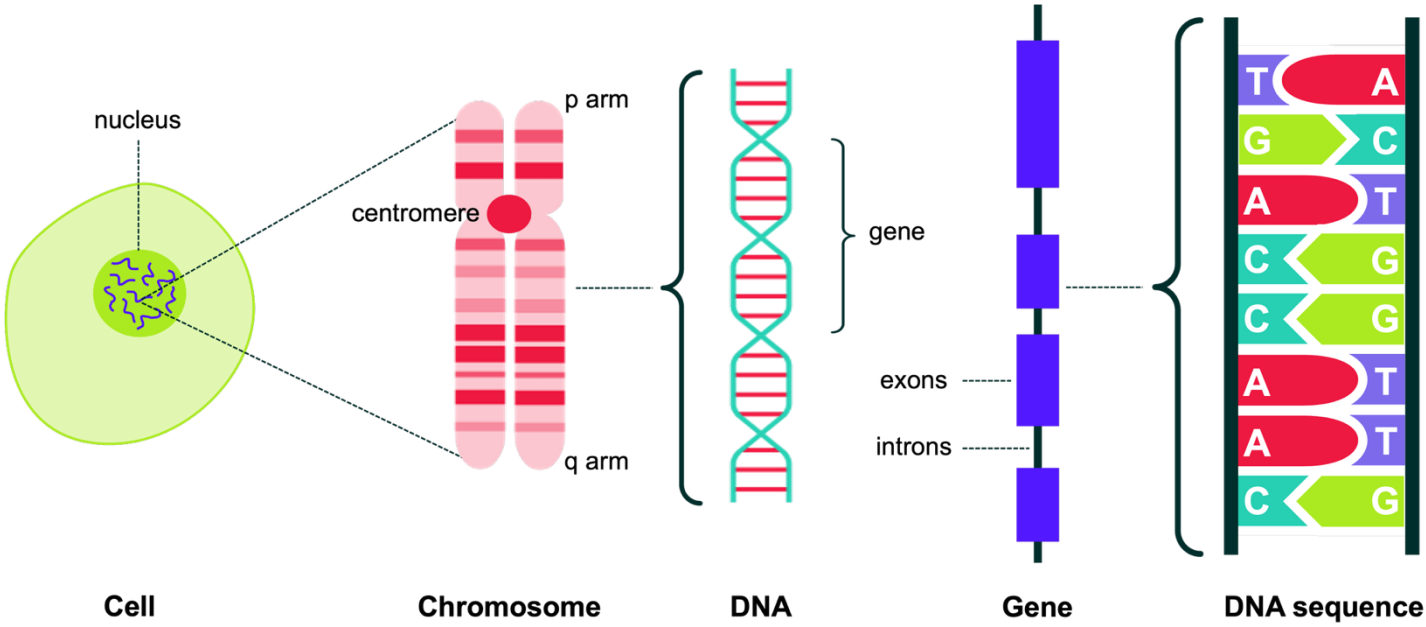
It is very important to distinguish Cockayne syndrome from the separate disorder of Adult Xeroderma Pigmentosum-Cockayne syndrome Complex, where malignancy is a feature.

This section includes some more complicated scientific terms and concepts - don't worry if it's a lot to take in, you can always come back to this section later if you want to.

Genes and chromosomes

Genes are instructions which have important roles in our growth and development. They are made of DNA and are incorporated into organised structures called chromosomes. Chromosomes therefore contain our genetic information. Chromosomes are located inside our cells, the building blocks of our bodies. In people with genetic conditions, one or more of their genes don't instruct the body as expected, which can lead to changes in how their body works.

DNA is made up of building blocks called 'bases' or 'nucleotides'. There are four DNA bases which can be abbreviated to the letters A, C, G, and T. These DNA bases are paired up in the DNA structure into 'base-pairs'. The full sequence of our DNA is over three billion base-pairs long. There are changes in the DNA sequence (variants) present in everyone's genes. It is variants in our genes that make each one of us unique individuals.

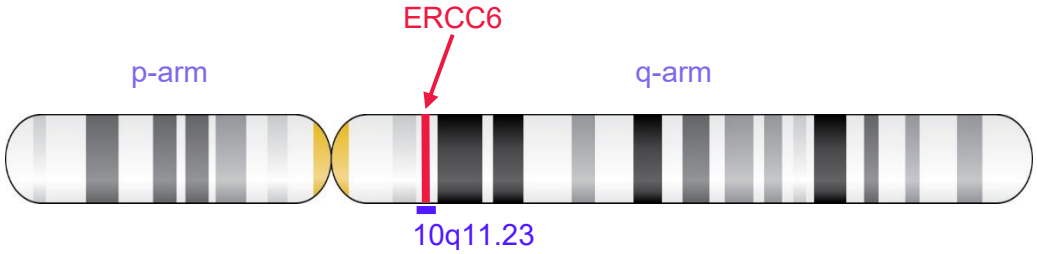


What causes Cockayne syndrome?

Cockayne syndrome is caused by specific changes (known as pathogenic variants) to the DNA sequence of a gene called ERCC6 (ERCC6 is an abbreviation of the gene's full name, ERCC Excision Repair 6, Chromatin Remodeling Factor). The condition is also caused by pathogenic variants in a different gene called ERCC8. Variants in ERCC6 are more common; in a study of 124 individuals with Cockayne syndrome, 85 had variants in ERCC6 and 39 had variants in ERCC8 (Calmels 2018).

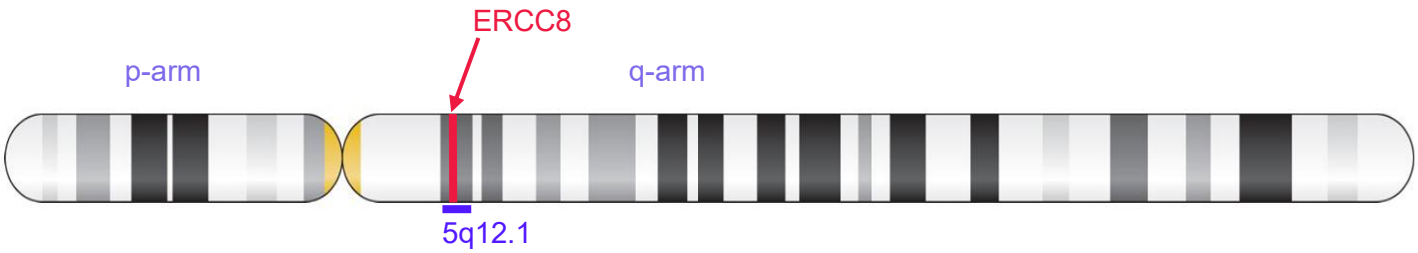
The ERCC6 gene is located in the long 'q' arm of chromosome 10 in a region called 10q11.23 as shown in the image below.

Chromosome 10



The ERCC8 gene (full name: ERCC Excision Repair 8, CSA Ubiquitin Ligase Complex Subunit) is located on the long ‘q’ arm of chromosome 5 in a region called 5q12.1 as shown in the image below.

Chromosome 5



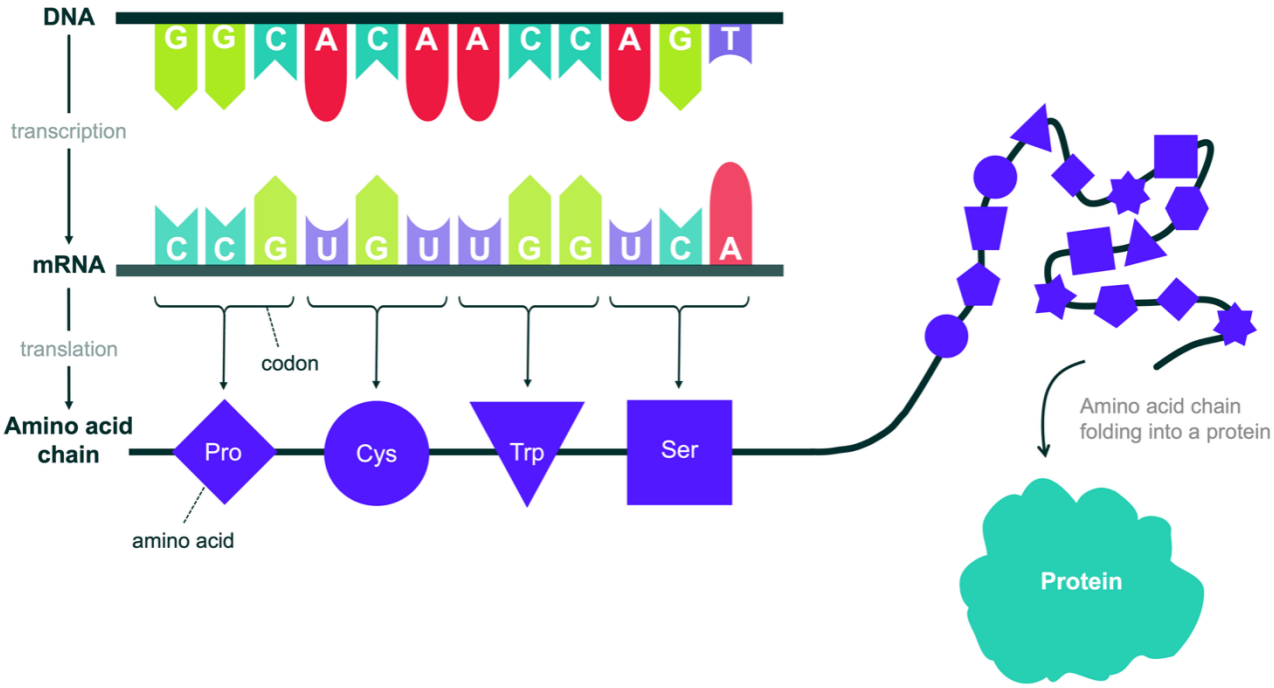
We have two copies of chromosome 10 in our cells, and two copies of chromosome 5, so we also have two copies of the ERCC6 and ERCC8 genes. Cockayne syndrome occurs when both copies of the ERCC6 or both copies of the ERCC8 gene are affected. This is known as autosomal recessive since all numbered chromosomes are called autosomes and genetic conditions that occur when both copies of an autosomal gene are affected are known as recessive.

Unique publishes a separate guide to single gene disorders – autosomal recessive inheritance

Cockayne syndrome can also be caused by deletions of both copies of the ERCC6 or ERCC8 genes (or part of the genes) but this is less likely to happen to both copies of a chromosome. In very rare circumstances, it is possible to have a deletion of the gene on one chromosome and a gene variant on the other chromosome.

Unique publishes a separate guide to deletions and microdeletions

Most genetic conditions are caused by changes to genes that provide instructions for making proteins; these are called protein-coding genes. ERCC6 and ERCC8 are two of thousands of these protein coding genes. Proteins are molecules that are made up of long chains of chemicals called amino acids and play critical roles in the body. This is because proteins are essential for lots of processes such as breaking down food, moving our muscles, and growing the body’s organs and making sure they function properly. To make these amino acids a copy of the DNA sequence is created, called messenger RNA (mRNA). mRNA uses the same A, C and G bases as DNA, but the ‘T’ bases are swapped to ‘U’ bases. Within a gene, each three-letter sequence (codon) of mRNA bases provides the instructions for one amino acid (as shown in the image below). Changes to the amino acid sequence can affect the function of the protein.



The proteins made by the ERCC6 and ERCC8 genes play a primary role in a DNA repair pathway that removes DNA damage, particularly from ultraviolet (UV) radiation and a type of cellular stress called oxidative stress. Pathogenic variants in either gene lead to the production of non-functional proteins, and a loss (deletion) of the gene sequence means no protein is made. This affects the DNA repair pathway, causing an accumulation of DNA damage which results in cells dying before they usually would. This impaired DNA repair is a key feature of Cockayne syndrome.

The role of the CSA protein

The ERCC8 gene sequence is used to make the Cockayne syndrome A (CSA) protein, and the ERCC6 gene sequence is used to make the Cockayne syndrome B (CSB) protein. These proteins are important because they are multi-functional and crucial for maintaining the health of cells and the stability of DNA. Their main role is in a process called Transcription-Coupled Nuclear Exision Repair (TC-NER), which repairs DNA damage. When this DNA repair process does not work correctly, damage can build up in cells that do not divide, such as brain cells (neurons), which can lead to the severe neurological symptoms seen in individuals with Cockayne syndrome. This also helps to explain why skin, hair and eyes are vulnerable to sun exposure. Other functions include protecting cells from damage caused by byproducts of typical metabolism (oxidative stress), helping to clear away parts of our cells that are damaged (mitochondria, the organelle responsible for energy production) and helping to regulate the activity of many other genes.

Unlike some other conditions involving DNA repair, Cockayne syndrome is not associated with an increased risk of cancer. This is because cells with significant DNA damage are more likely to undergo programmed cell death (apoptosis) instead of turning into cancer cells. While this prevents cancer, it contributes to the premature ageing and tissue degeneration that are characteristic of the syndrome.

Different types of genetic changes

The specific type of genetic change in the ERCC8 or ERCC6 gene is an important factor that could influence an individual's symptoms and features. Research suggests that different types of variants can affect the CSA or CSB protein in different ways, which might account for the variability in symptoms and features, or their severity, in different people with Cockayne syndrome. Variants in ERCC6 are found in approximately two thirds of individuals with Cockayne syndrome, while ERCC8 variants account for about one third.

Gene Sequence Variants, Loss of Function (LOF): People with Cockayne syndrome are more commonly found to have a gene sequence variant, as opposed to a deletion of the entire gene. The pathogenic variants identified in both genes are primarily protein-truncating. Such variants include:

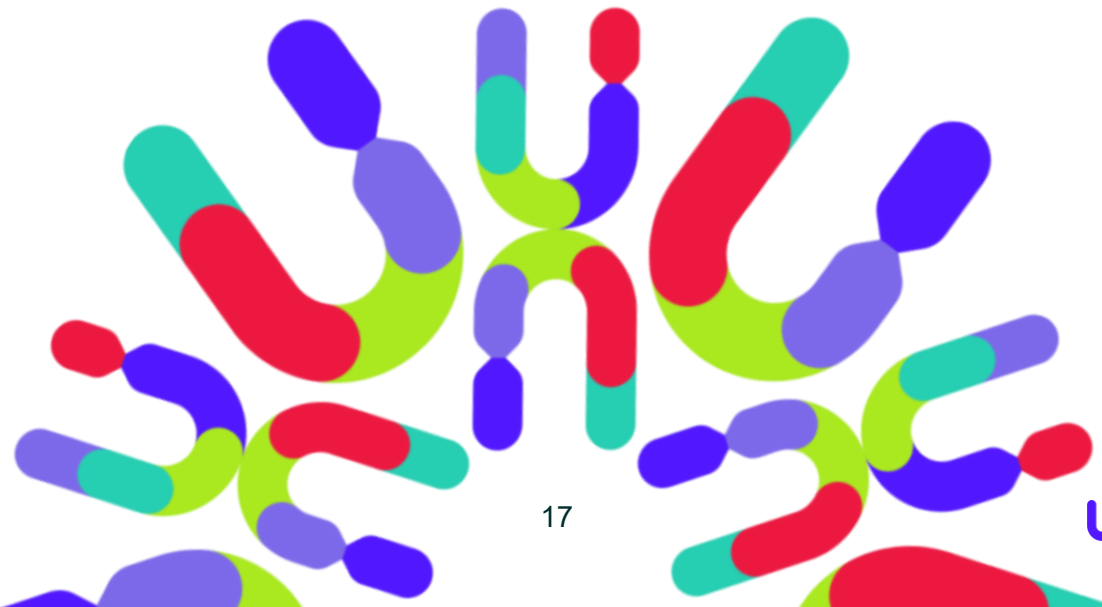
- Nonsense variants: Where the amino acid change results in a premature 'stop' signal, stopping protein production too early, leading to a shorter, unfinished (truncated) protein
- Frameshift variants: Where the DNA coding sequence is shifted by the addition or deletion of individual DNA bases which means the incorrect amino acid sequence is used to produce the protein or there is a premature 'stop' signal
- Splice-site variants: Which affect how the gene's instructions are pieced together, leading to a shortened or altered protein
- Missense variants: Where one amino acid is replaced by another, producing an altered protein

These variants are often thought to be loss of function variants (LOFs), because they lead to shortened, non-functional, or unstable proteins, or disrupt the protein's usual structure and function.

Genetic Tests

Cockayne syndrome caused by gene sequence variants, can be identified by a type of genetic test called sequencing, such as whole exome sequencing (WES) or whole genome sequencing (WGS). Gene deletions can also be identified by a sequencing test but are more commonly found using a different type of genetic test called a chromosome microarray (CMA), also known as an arrayCGH or SNParray, or targeted gene deletion or duplication analysis e.g. Multiplex Ligation-dependent Probe Amplification (MLPA).

Unique publishes separate guides to DNA sequencing, arrayCGH and SNParrays



Genetic Test Results

The results of genetic (genomic) testing are likely to be provided by a geneticist, a genetic counsellor or the clinician who ordered the test. Depending on the test that was carried out, someone with a Cockayne syndrome might have results that look like one of these examples/the following example:

An example result of a DNA sequencing test (e.g. WES or WGS), that can identify gene variants, is shown here for the ERCC6 gene:

p.Arg735Ter (C>T): c.2203C>T ERCC6 (735 R/*) (NM_000124.4)

p. Arg735Ter	signifies the change to the protein: the amino acid Arginine (Arg) has been replaced by a stop (termination) signal (Ter) to stop the addition of another amino acid to the growing protein chain. This occurred at position 735 in the sequence of amino acids that make up the protein
C>T	signifies the gene sequence change: the C nucleotide has been replaced by a T nucleotide
c.2203	signifies the base pair position of the change within the gene's coding sequence (the position where the C nucleotide has been replaced by the T nucleotide)
ERCC6	signifies the gene that is affected
735 R/*	signifies that the amino acid Arginine (R) at position 735 of the protein has been replaced by a stop codon (*)
NM_000124.4	this is the specific 'reference sequence' or blueprint of the gene that scientists use to identify the location of the variant

The result of a chromosome microarray (CMA) test (e.g. arrayCGH or a SNParray), that can identify deletions and duplications, is shown here for a microdeletion within band 10q11.23:

arr[hg19] 10q11.23 (50,713,464_51,043,557)x1 dn

arr	the analysis was by array (arr) comparative genomic hybridisation (cgh)
hg19	Human Genome build 19. This is the reference DNA sequence that the base pair numbers refer to. As more information about the human genome is found, new 'builds' of the genome are made, and the base pair numbers may be adjusted. This means base pair positions change depending on the assembly used
10q11.23	The chromosome involved is chromosome 10 and the position of the deletion is in band q11.23
48282039-49876096	base pairs between 48,282,039 and 49,876,096 have been shown to be deleted. Take the first long number from the second and you get 1,594,057 (1.594Mb).This is the number of base pairs that are deleted
x1	means there is one copy of these base pairs, not two – one on each chromosome 2 – as you would normally expect, so this a deletion
dn	means *de novo*. The biological parents' chromosomes have been checked and no deletion or other chromosome change has been found at position 10q11.23. The deletion is very unlikely to be inherited and has almost certainly occurred for the first time in this family with this child mat here would mean that the deletion has been inherited from the biological mother pat here would mean that it has been inherited from the biological father

Unique publishes a separate guide to Interpreting Genetic Test Results

Why did this happen?

In almost all people identified so far (2026) with Cockayne syndrome, both parents passed on a copy of the ERCC8 (associated with Cockayne syndrome type A) or ERCC6 (associated with Cockayne syndrome type B) gene containing a variant to their child with Cockayne syndrome, so one variant was inherited from the biological mother and one from the biological father. There is nothing that happened before or during the pregnancy that caused this to happen. We all have small changes in our genes, and it is by chance that two parents have alterations in the same gene, or because the parents share a common ancestor. It is important to recognize that no one should be blamed for variants in their DNA and no parent is at fault when DNA changes are present in their child.

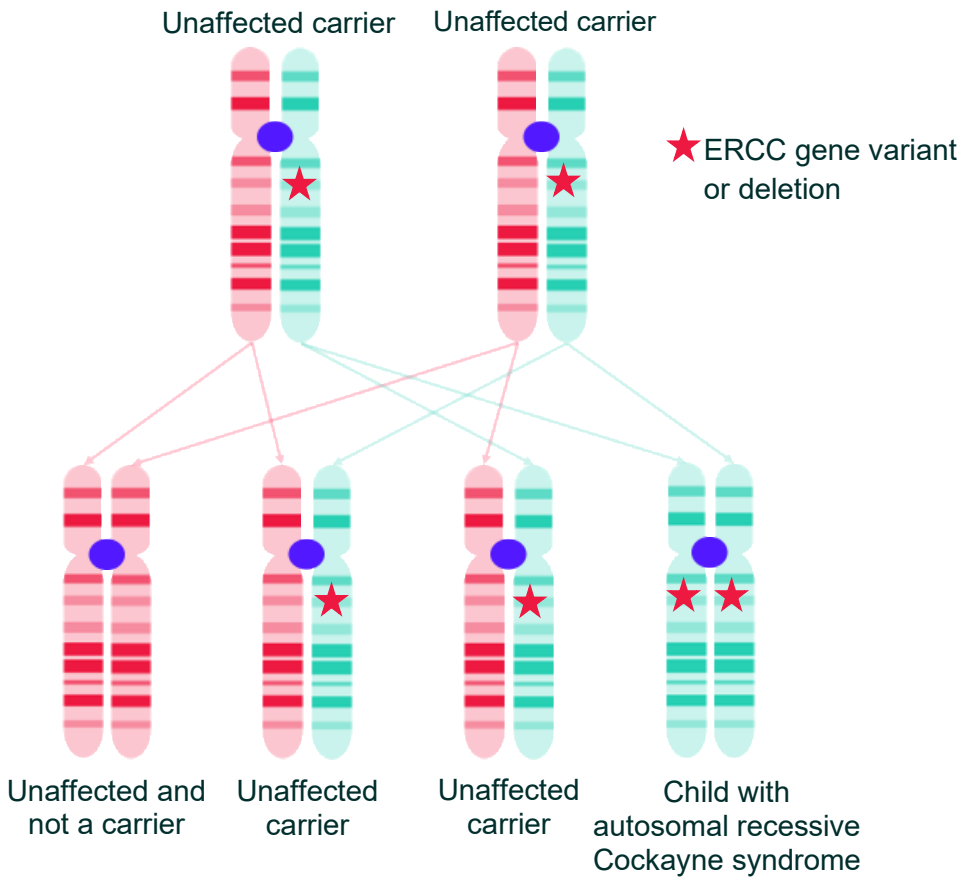
For many genes, including the ERCC8 and ERCC6 genes, having only one copy of the fully functional gene is enough for the body's healthy functioning. Therefore, when parents have only one copy of the ERCC8 or ERCC6 gene with a variant or deletion, they are typically unaffected and do not know they are carriers of the genetic change. Cockayne syndrome only occurs if both copies of the ERCC8 or ERCC6 gene contain a variant and/or are deleted.

Very rarely children and adults are identified as having recessive genetic variants in both copies of a particular gene, but the genetic changes are different, this is known as compound heterozygosity. Some individuals may carry a gene variant in one copy of a gene and the other copy may be affected in a different way, such as a different change in the code, or the gene being partially or fully absent due to a deletion or altered due to a chromosomal rearrangement or duplication. For example, a person might inherit a deletion of a small part of the ERCC6 gene from one parent and a different type of variant (e.g. a nonsense variant) from the other parent or they may be chance have a variant or deletion not found in either parent.

Inheriting two identical copies of a variant is known as homozygosity. In some conditions associated with consanguinity (when parents are related by blood, e.g. first cousins), genomic testing may show runs of homozygosity, where both parents share common ancestry and pass down identical regions of DNA.

Can it happen again?

The possibility of having another child affected by a rare autosomal recessive gene disorder depends on the genetic code of the parents. If both parents are known to carry a variant in the ERCC6 or ERCC8 gene, theoretically there is a one in four (25%) chance their child would have Cockayne syndrome, a one in two (50%) chance their child would be an unaffected carrier (like their parents) and a one in four (25%) chance of their child being unaffected and not a carrier. This chance resets for each pregnancy.



The biological parents of a child with Cockayne syndrome are almost always carriers of the condition. Carriers are typically not at risk of developing the disorder themselves; however, a rare phenomenon has been reported where some carrier parents manifested mild features.

All the biological children of a person with Cockayne syndrome will be unaffected carriers of the pathogenic variant inherited from the person with Cockayne syndrome unless the person with Cockayne syndrome has biological children with someone who also has Cockayne syndrome or is a carrier of a pathogenic variant for Cockayne syndrome. Individuals with the more severe forms of Cockayne syndrome (types I and II) are not likely to have a family of their own, so this is most relevant for individuals with the milder type III.

Once a person has been diagnosed with Cockayne syndrome, genetic testing can be carried out on relatives who may also carry the pathogenic variant in the ERCC6 or ERCC8 gene, including siblings of an affected child who should be tested as soon as possible after they are born. Siblings of an affected individual have a one in two (50%) chance of being a carrier. Each sibling of the parents has a 50% chance of also being a carrier. There is testing that can be done, such as prenatal testing (chorionic villus sampling or amniocentesis) and preimplantation genetic testing (PGT), and technology can be used to greatly decrease the risk of having another affected pregnancy.

A clinical geneticist or genetic counsellor can provide specific advice for each family about the chance of having further children with Cockayne syndrome.

Can Cockayne syndrome be cured?

There is no cure for Cockayne syndrome. Management of the condition is through supportive care, with the main goals being to improve quality of life, maximise function and reduce complications. Knowing the diagnosis means that appropriate monitoring and interventions can be put in place. Management is comprehensive and involves a team of different specialists. Examples of interventions and monitoring include:

- Support with growth and nutrition, which can include a feeding tube (gastrostomy)
- Individualised educational programmes and therapies, including occupational, physical and speech therapy
- Medications to manage symptoms such as tremors and spasticity
- Standard treatments for vision and hearing issues, such as hearing aids or cochlear implants
- Regular dental care to minimise cavities
- Regular surveillance of diet, nervous system function, vision, hearing and blood pressure

It is also important to avoid excessive sun exposure and the antibiotic metronidazole (due to liver problems). Caution is also advised with some other medications.

Management

The following suggestions have been provided by clinicians, who have personal experience of managing/treating individuals with Cockayne syndrome, to improve quality of life and reduce complications. The Cockayne syndrome natural history study (Wilson 2016) recommends a detailed surveillance schedule and the Cockayne syndrome GeneReviews® (Laugel 2024) suggests management options.

Children and adults with Cockayne syndrome should be under the care of a multidisciplinary team. The team should include a geneticist and paediatrician (for children) who can oversee care so that development and behaviour can be monitored, and the best help given in the form of different therapies. Individuals may also have evaluations with various specialist doctors.

Immediately following diagnosis

When not carried out as part of the diagnostic process, an evaluation of the features of Cockayne syndrome that are present in the child or adult who has been diagnosed with this genetic condition is recommended. This can determine which of the features of Cockayne syndrome are present and how severe they are.

The following assessments are recommended:

- A physical examination to look for features such as growth failure, feeding difficulties, skin photosensitivity, dental cavities (caries) and skeletal changes including joint contractures or scoliosis. This should include plotting growth on specialised growth charts
- A developmental assessment to evaluate motor, adaptive, cognitive and speech-language skills to determine the need for early intervention programmes (including occupational, physical, speech and feeding therapy)
- An eye (ophthalmologic) assessment to check for cataracts, retinopathy or retinal dystrophy
- A heart (cardiac) assessment to look for high blood pressure (hypertension) and poor peripheral circulation
- A hearing (audiological) assessment to determine the severity of hearing loss and ensure early intervention

- A neurologic assessment to determine whether conditions such as weakness, an atypical gait and learning (intellectual) disability are present. Brain magnetic resonance imaging (MRI), a technique that can be used to visualise the brain, should be carried out as changes to the white matter of the brain are a known feature of Cockayne syndrome
- Laboratory tests to assess kidney and liver function

Genetic counselling for affected individuals and their families should also be offered including signposting to family support and resources, which can include community resources, social work support and home nursing referrals.

Supportive care

How a person with Cockayne syndrome is cared for is likely to require co-ordinated care by a multidisciplinary team of specialists, which may include:

Paediatrician – a doctor who specialises in the physical, mental and social health of children from birth to young adulthood

Developmental Paediatrician – a doctor who specialises in child development and can help with behaviour management

Geneticist and Genetic Counsellor – a specialist who can confirm the diagnosis and provide information and advice on the genetic nature of the condition

Neurologist – a doctor who specialises in conditions of the brain, spinal cord and nervous system

Cardiologist – a doctor who specialises in heart conditions

Nephrologist – a doctor who specialises in conditions affecting the kidneys

Hepatologist – a doctor who specialises in conditions affecting the liver

Ophthalmologist – a doctor who specialises in conditions affecting the eyes

Audiologist – a health care professional who diagnoses, treats and helps manage a condition that involves hearing or balance

Dentist – a healthcare professional who provides care for the teeth and gums

Dietitian – a healthcare professional who can advise on nutrition and help manage feeding difficulties

Occupational therapist (OT) – a health care professional who uses activities to aid self-management of a condition and can provide equipment

Physiotherapist/physical therapist (PT) – a health care professional who uses exercise, movement, manual therapy, education and advice to help with the body's strength and mobility

Speech and language therapist (SALT) – a health care professional who helps with speech, language communication and sometimes feeding and swallowing difficulties

Specialist nurses and/or **other healthcare professionals** may need to systematically and comprehensively plan a child or adult's treatment.

Treatments and therapies

Early intervention can be beneficial and formal testing to assess specific, individual needs is recommended. An education, health and care plan (EHCP) in the UK, individualized education plan (IEP) in the US, or equivalent document in other countries, may be issued after a child has undergone an assessment, to help ensure that the educational, health and social provisions deemed necessary to support the child's needs are delivered.

As there is no cure, management is supportive and focuses on improving quality of life through a multidisciplinary team approach. Treatment will depend on the specific features and symptoms experienced by the person with Cockayne syndrome but may include:

Physiotherapy to manage low muscle tone (hypotonia), joint stiffness (contractures) and spasticity. Therapists also assist with mobility and may recommend adaptive equipment such as walkers, wheelchairs, orthotics and splints.

Occupational therapy for fine motor skill delays, which can include activities to improve hand strength and coordination for daily tasks (e.g. feeding, dressing, grooming and writing).

Speech therapy for a range of speech and language delays or difficulties and feeding/swallowing difficulties. This may include modifying food by thickening or chilling it to improve safety. For children with moderate to severe difficulties, this can include regular sessions focusing on Augmentative and Alternative Communication (AAC) methods (e.g. sign language, picture exchange systems and high-tech communication devices) and provides a functional means of communication for individuals who are non-verbal or have very limited speech.

Behavioural therapy for features of autism, which can include structured therapies like Applied Behaviour Analysis (ABA) to help manage challenging behaviours, improve social skills and develop coping strategies.

Vision support, which includes regular eye examinations to monitor for cataracts and changes in the retina (retinopathy). Due to light sensitivity (photophobia), sunglasses are recommended outdoors.

Hearing support, as hearing loss is common. Regular hearing tests are recommended, and management may include hearing aids, cochlear implants or bone-anchored hearing aids.

Dental care, as individuals can be prone to tooth decay (dental caries), making proactive dental care essential.

Skin protection, as the skin is highly sensitive to the sun. Using high-factor sunscreen and limiting sun exposure are very important.

Medications may be prescribed such as baclofen, tizanidine, and Botox injections to manage spasticity; carbidopa-levodopa to treat tremor; proton pump inhibitors for gastroesophageal reflux (GERD); and amlodipine or ACE inhibitors for high blood pressure (hypertension).

Surgery, such as standard ophthalmological procedures to treat cataracts, or the placement of a gastrostomy tube (G-tube) for severe, long-term feeding difficulties to ensure adequate nutrition.

Important Considerations

There are some medications and treatments that should be used with caution or avoided completely:

- The antibiotic metronidazole must be avoided as it can cause severe liver failure
- A heightened response to opioids and sedatives is common, so extra care is needed and doses may be reduced
- Excessive sun exposure is avoided due to photosensitivity
- Treatment with growth hormone is not recommended

Surveillance

It is recommended that the following evaluations are carried out/considered to monitor an individual's existing symptoms, how they respond to care and treatment and whether any new symptoms emerge over time:

- Monitor for growth and adequate nutritional intake (a dietary assessment is recommended every six months, or more frequently if needed; growth should be plotted on charts specific to CS types I & II)

- Comprehensive developmental assessments (motor, adaptive, cognitive and speech-language skills) to determine the need for special education services; an evaluation for augmentative and alternative communication (AAC) devices should be considered for communication difficulties
- Regular dental check-ups
- Consider a palate review (particularly if there are feeding difficulties or speech concerns); oral motor function should be reassessed at each visit, with swallowing studies performed if there are signs of choking, poor weight gain or frequent respiratory illnesses
- Consider an annual cardiac review (including monitoring blood pressure)
- Consider annual audiologic assessments (or more frequently if needed)
- Consider a neurologic review (including an MRI at diagnosis, and evaluation of gait, muscle tone and overall functioning at every visit)
- Consider a skeletal review (with radiographs if clinically indicated)
- On-going examinations by an ophthalmologist are recommended every six months until the age of four, and then annually (to check for cataracts and retinopathy)
- Kidney function should be monitored annually (including tests for uric acid and proteinuria)
- Liver function should be monitored annually (with tests for liver enzymes)
- Check blood glucose annually
- Consider a dermatologic evaluation for skin issues
- Assessment of the need for social support, such as home nursing care, community resources and social work or genetic counselling

Research into new treatments for Cockayne

The genetic change causing Cockayne syndrome affects development of the brain and other parts of the body before birth. Therefore, a complete cure is unlikely, even in the future, since the brain has already formed by the time a diagnosis is made. However, research into improved treatments and management for various features of Cockayne syndrome is ongoing. In addition, although Cockayne syndrome is a relatively rare effects of variants in these genes which impair a DNA repair process called transcription-coupled nucleotide excision repair (TC-NER). The loss of protein function is also linked to other cellular problems, such as oxidative stress and mitochondrial dysfunction, which are believed to be major contributors to the features of the condition.

One avenue of research is to identify drugs that can help with the downstream effects of the affected genes. A promising pre-clinical study has shown that serine protease inhibitors were able to reverse mitochondrial defects in cells from individuals with Cockayne syndrome. This identifies a potential therapeutic pathway, though further research is required to assess its safety and efficacy in humans.

Another potential future strategy is gene therapy. The goal would be to introduce a correct copy of the faulty gene into an individual's cells to restore protein function. However, this research is in its infancy, with no active clinical trials, and there are significant challenges to overcome, particularly in developing safe and effective methods to deliver the gene to all the necessary cells in the body, especially the brain.

Details of clinical trials related to a particular condition or gene can be found at **ClinicalTrials.gov** and **EU Clinical Trials Register**.

The US based Cockayne Syndrome Foundation publishes their own excellent resources including a Caregiver Manual and Healthcare Provide Manual.

Sources

The information in this booklet is drawn from the published medical literature and information from Unique members. The first-named author and publication date for articles in the medical literature are given to allow you to look for the abstracts or original articles on the internet in PubMed (**pubmed.ncbi.nlm.nih.gov/**).

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Inform Network Support

Rare Chromosome Disorder Support Group
The Stables, Station Road West, Oxted, Surrey, RH8, 9EE, UK
Tel: +44(0)1883 723356
help@rarechromo.org I rarechromo.org

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Websites:

- Amy and Friends
- The Cockayne Syndrome Foundation
- Share & Care Cockayne Syndrome Network, Inc.
- Viljem Julijan Association
- Riaan Research Initiative
- National Initiative for Cockayne Syndrome

This guide was reviewed by Dr Isabella Leung Lai-Ting, Resident, HKCH Department of Clinical genetics (DCG), Hong Kong Children's Hospital, Hong Kong SAR, China.

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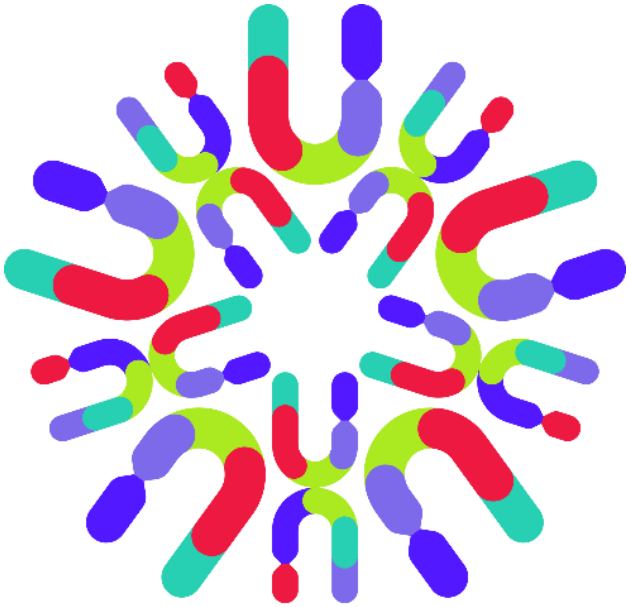

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