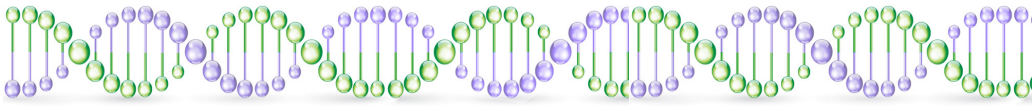
Information Sheet



Gorlin Syndrome (Nevoid Basal Cell Carcinoma syndrome) and the PTCH1 and SUFU genes

What is Gorlin syndrome?
Gorlin syndrome is caused by a germline mutation in the PTCH1 gene and less commonly, the SUFU gene. It is rare, affecting around 1 in 30,000 people. Gorlin syndrome is also known as Nevoid Basal Cell Carcinoma syndrome (NBCCS). Other terms that have been used include multiple basal-cell carcinoma syndrome and Gorlin–Goltz syndrome.

What are the signs and symptoms of Gorlin syndrome?
Individuals with Gorlin syndrome develop a type of skin cancer called basal cell carcinoma (BCCs). BCCs are common, particular on sun damaged, fair skin. However, in Gorlin syndrome BCCs may occur at a very young age and, in some people, hundreds or even thousands of BCCs may develop over a lifetime.

The signs and symptoms of Gorlin syndrome vary greatly from individual to individual, even in the same family.

How is Gorlin syndrome (Nevoid Basal Cell Carcinoma syndrome) diagnosed?
Gorlin syndrome is diagnosed clinically. The signs are grouped into major criteria and minor criteria, with 2 major and 1 minor criteria or 3 minor criteria resulting in a clinical diagnosis. Genetic testing is recommended. Individuals with major criteria or a rare minor criterion should seek further assessment.

The major criteria for clinical diagnosis of Gorlin syndrome (Nevoid Basal Cell Carcinoma syndrome) are:

- calcification of the falx cerebri
- keratocystic odontogenic tumours
- palmar / plantar pits
- a basal cell carcinoma before age 30 or multiple BCCs (>5 if in England, may be more for Australia!)

The minor criteria for clinical diagnosis of Gorlin syndrome (Nevoid Basal Cell Carcinoma syndrome) are sometimes very rare in the general population while others are relatively common. They include:

- Medulloblastoma (primitive neuroectodermal tumour)
- Cardiac fibroma or ovarian fibroma
- unusual appearance of the ribs and/or the spine such as bifid ribs seen on X-ray
- cysts in the lung
- a cleft lip or cleft palate
- extra fingers or toes (polydactyly)
- wide-spaced eyes (hypertelorism) or changes the iris or retina (coloboma)

What is calcification of the falx cerebri?
Almost all individuals with Gorlin syndrome aged over 20 will have calcification of the falx cerebri. The falx cerebri is a membrane separating the hemispheres of the brain. Calcification of the falx cerebri doesn't cause problems but shows up on a skull X-ray.

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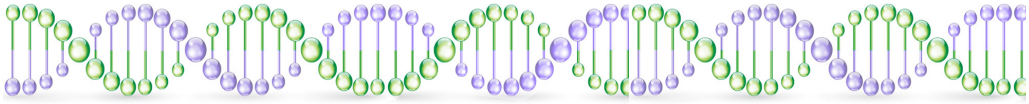

What are Keratocystic Odontogenic Tumours?
Cysts in the jaw (keratocystic odontogenic tumours) are also common in Gorlin syndrome and appear before age 30. Keratocystic odontogenic tumours can cause swelling and tooth displacement. If these cysts are seen on a jaw X-ray, the likelihood of finding a mutation in the PTCH1 gene is ~50%.

What are Palmer Plantar Pits?
Many individuals with Gorlin syndrome have punched out areas that appear on the palms of the hand or the soles of the feet, particularly after soaking in water. This is referred to as "pitting" and is harmless.

What is a Primitive Neuroectodermal Tumour (PNET)?
A primitive neuroectodermal tumour (PNET) is a rare brain tumour. It is also known as a medulloblastoma. Medulloblastoma arise in embryonal tissue that continues growing rather than becoming the adult form. They occur in the cerebellum but can spread elsewhere in the brain or spinal cord.

Medulloblastoma are grouped according to the genetic mistake(s) that allows them to grow. In Gorlin syndrome, the SHH (Sonic Hedgehog) pathway is the most likely affected. Other causes include the MYC pathway, the NOTCH1 pathway and the WNT pathway. Activation of the WNT pathway is the most common cause of medulloblastoma and in some cases this is associated with an inherited mutation in the APC gene associated with Familial Adenomatous Polyposis syndrome (sometimes called Turcot syndrome).

In Gorlin syndrome, if a primitive neuroectodermal tumour (PNET or medulloblastoma) occurs, it happens at a young age. A child diagnosed with a medulloblastoma that has a SHH molecular subtype has greater than 11% chance of carrying a germline SUFU mutation and an 8% chance of a PTCH1 mutation. Around 5% of children with Gorlin syndrome (Nevoid Basal Cell Carcinoma syndrome) develop medulloblastoma.

What are cardiac and ovarian fibromas?
A non-cancer growth, called a fibroma, may occur in the heart in around 2% of individuals with Gorlin syndrome. Fibromas may also occur in the ovary in 20% of women with Gorlin syndrome (note: this doesn't affect fertility).

How is Gorlin syndrome managed?

- Management involves a dental review with jaw X-ray from age 8 and a once-off ultrasound of the heart to exclude a cardiac fibroma as a baby.
- Sun protection is very important. Skin examinations start at age 10 and when basal cell carcinomas occur, standard treatments are used.
- Because mutations in the SUFU gene have a strong association with medulloblastoma in childhood, brain MRI screening is recommended every 4 to 6 months from 4 months of age to age 5

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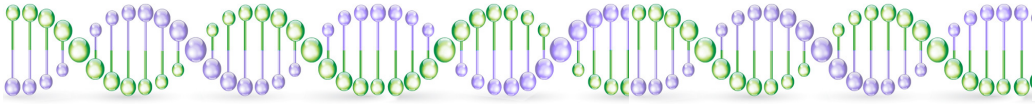

Is Gorlin syndrome, also known as Nevoid Basal Cell Carcinoma syndrome, inherited?
Yes. Gorlin syndrome is a hereditary cancer syndrome caused by mutations in the PTCH1 or SUFU genes.

There is a 50% chance of a person who carries a germline PTCH1 or SUFU mutation, whether male or female, passing the mutation to their son or daughter. If a mutation is identified, then predictive testing is available for blood relatives.

Does this sound like you or your family?
Have you been told you have keratocystic odontogenic tumours or calcification of the falx cerebri? Has a PTCH1 or SUFU mutation been detected in a blood relative?

Genetic testing is available. Make an appointment with Dr Hilda High at Sydney Cancer Genetics. It is a confidential opportunity to discuss your personal and family history of cancer and genetic testing can be organised, if needed.

More information is available on our website, including links to the following:

- Support groups exist in Australia, the UK and the USA among others.
- If you want to participate in research into Gorlin syndrome, you can join the international registry. More information is available on the Gorlin Syndrome Alliance website
- The Cancer Genetics section of the Cancer Institute's eviQ website provides up-to-date Australian-based management guidelines
- The US National Library of Medicine website has more information about this syndrome.

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