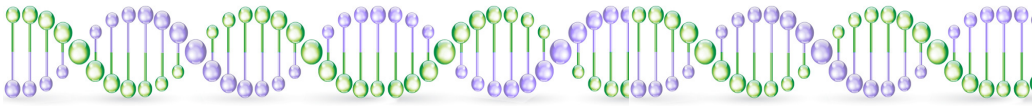
Information Sheet



Familial Adenomatous Polyposis and the APC gene

Familial Adenomatous Polyposis (FAP), as the name suggests, causes polyps. It affects 1 in 7,000 to 1 in 22,000 people.

What is Familial Adenomatous Polyposis syndrome?
In the classic form, 100s to 1000s of adenoma (polyps) develop in the colon (bowel). These polyps start appearing in childhood and left untreated these polyps almost always become cancerous. The classical form is associated with a phenotype that includes desmoids, cysts in the jaw (osteomas), changes in the eye (CHRPE) and polyps elsewhere in the gastrointestinal tract.

There is also a milder form called attenuated FAP (AFAP). Here, 10s to 100s of polyps develop. The polyps usually appear in the 20s or older and there are usually no other signs or symptoms.

What are Adenomatous polyps?
Adenomatous polyps (adenoma) are the most common kind of polyp found in the bowel. If you have had a few polyps removed in your 50s or 60s, don't panic! It is quite common to have a few adenomatous polyps. On average, it takes 10 years for a polyp to become a cancer. That is why bowel cancer screening starts at 50 in the general population.

What is Adenomatous Polyposis?
Definitions of polyposis vary and are based on polyp type and number as well as age of onset and even location. If you have had more than 20 adenoma or if there were 5 to 10 polyps but they were detected in your 20s or 30s, it would quality as polyposis and you could have Familial Adenomatous Polyposis syndrome or attenuated FAP.

Other names for Familial Adenomatous Polyposis syndrome
Before it was known that germline (heritable) mutations in the APC gene were responsible for FAP, Familial Adenomatous Polyposis syndrome was known by other names, based on the clinical features.

> **Gardner syndrome** is a clinical syndrome used to describes families with multiple bowel polyps (adenomas of the colon) and skin lumps such as epidermoid cysts or lipomas, desmoids (tumour of the connective tissues) and osteomas (benign bone growths, often found in the jaw). It's an old term and no longer used. Gardner syndrome also applied to families with Lynch syndrome who had sebaceous adenocarcinomas of the skin.
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> **Turcot syndrome** is a clinical syndrome used to describe families with multiple bowel polyps (adenomas of the colon) and brain tumours. When the genetic cause is an APC mutation, such as in Familial Adenomatous Polyposis syndrome, the brain tumours are usually medulloblastoma. Turcot syndrome also applied to families with Lynch syndrome but in these families the brain tumours were usually glioblastoma.

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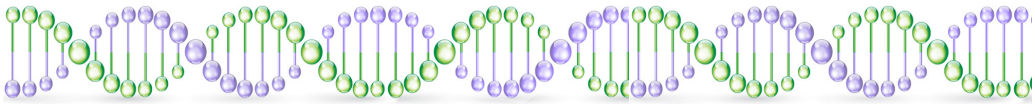

What is special about the APC c.3920T>A mutation?
A particular mutation in the APC gene, written APC c.3920T>A p.(Ile1307Lys), is common in people of Ashkenazi Jewish descent. Rather than switching on the APC gene and causing multiple polyps to grow, this mutation increases the chance that more mistakes will occur in the APC gene itself in bowel cells over time (somatic mutations). It occurs in 6 to 11% of individuals with Ashkenazi heritage.

In the Ashkenazi Jewish population the APC c.3920T>A mutation has been shown to result in a moderately increased risk of colorectal cancer. Guidelines recommend starting bowel cancer screening at age 40 with faecal occult blood testing (FOBT) and commencing colonoscopy screening every 5 years from age 50, although this may change with the particular family history.

A rare type of thyroid cancer associated with Familial Adenomatous Polyposis syndrome
Thyroid cancer is not common in individuals with Familial Adenomatous Polyposis syndrome. However, when it does occur, it's usually a rare type called a cribriform-morular variant of papillary thyroid cancer. Germline genetic testing is recommended for everyone who has this rare kind of papillary thyroid cancer.

Management of Familial Adenomatous Polyposis syndrome
Screening starts at a young age in FAP. That is why genetic testing is performed in children. The polyps can occur at a very young age and these polyps, if not removed, can become cancer. The risk is almost 100% by age 40, with some bowel cancers even occurring in childhood.

- In classical FAP screening starts at age 10 or 12 with a flexible sigmoidoscopy or colonoscopy performed every year.
- For attenuated FAP, screening starts at age 18 and may be done every 2 to 3 years until polyps are detected.
- Colectomy (surgical removal of the colon) is required when polyp load becomes too high to manage. This is usually around age 18 in classical FAP.
- Because the polyps can also occur elsewhere in the digestive tract, screening of the stomach and duodenum (beginning of the small intestine) with an endoscopy is required. This starts at age 25.
- There is no evidence that screening for the other cancers or growths, including hepatoblastoma, thyroid cancer or desmoids is helpful or saves lives.

Who should have genetic testing for Familial Adenomatous Polyposis syndrome?
Medicare funded testing is available for individuals with adenomatous polyposis and a 10% chance of carrying an APC mutation. This would include:

- having a total of 10 or more adenomatous polyps in the colon before age 30
- having a total of 20 or more adenomatous polyps in the colon before age 60

Even in the absence of polyposis, genetic testing should be considered if someone is diagnosed with:

- the cribriform-morular variant of papillary thyroid cancer
- a desmoid tumour involving the abdomen who was diagnosed at 10 years or older
- hepatoblastoma at any age
- congenital hypertrophy of the retinal pigment epithelium (CHRPE) if there are unusual features such as being in both eyes
- multiple osteomas of the jaw, especially if CHRPE is also present

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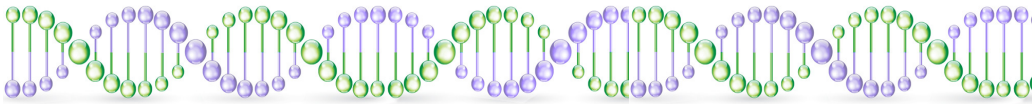

Is Familial Adenomatous Polyposis syndrome inherited?
Yes. Familial Adenomatous Polyposis syndrome is a hereditary cancer syndrome. There is a 50% chance of a person who carries a germline APC mutation, whether male or female, passing the mutation to their son or daughter. If a mutation is identified, then predictive testing is available for blood relatives. This testing is Medicare funded.

What are De Novo APC mutations?
In individuals with Familial Adenomatous Polyposis syndrome, 20% of the time, they are the first person in their family to carry an APC mutation. This is called a “de novo” mutation, meaning "from new". That is, the mutation occurred either in the making of that particular sperm or egg or the first few cell divisions after fertilisation. In this situation, the parents are not affected but the mutation can be passed on to the next generation.

Does this sound like you or your family?
Have you had multiple adenomatous polyps removed or has an APC mutation been detected in a blood relative? Medicare funded 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:

- We haven't found a specific Australian Support Group for this syndrome yet. However, FAP Gene Support Group is based in the UK and has good resources
- 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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