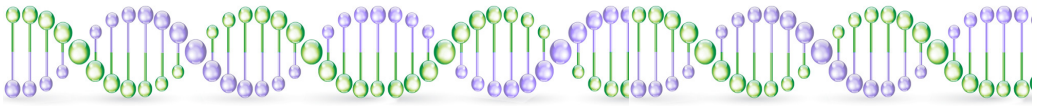
Information Sheet



Multiple Endocrine Neoplasia syndrome Type 1 (MEN1) and the MEN1 gene

Multiple Endocrine Neoplasia syndrome Type 1 affects 1 in 10,000 people. It is caused by a mutation in the MEN1 gene.

How is MEN1 diagnosed?
Multiple Endocrine Neoplasia syndrome Type 1 is characterised by combinations of more than 20 tumours involving the endocrine glands as well as non-endocrine tumours. Endocrine glands secrete hormones directly into the blood stream. Examples include the adrenal glands, the ovaries, the pituitary gland and the thyroid. The non-endocrine tumours include facial angiofibroma, lipomas and meningiomas.

To meet the clinical diagnostic criteria, an individual must have at least 2 of the key tumour types:

- Parathyroid tumour or hyperplasia (which manifests as primary hyperparathyroidism)
- Pituitary adenoma
- Well-differentiated neuroendocrine tumour of the gastro-entero-pancreatic tract

What is Primary Hyperparathyroidism?
There are 4 small parathyroid glands, which sit 2 on each side of the thyroid. They are important for keeping the calcium in the blood under steady control. Primary hyperparathyroidism occurs due to a growth within the gland itself while secondary hyperparathyroidism is simply the gland getting bigger in response to a calcium problem caused by another disease in the body (most commonly kidney disease).

Parathyroid tumours cause excess calcium to build up in the blood (hypercalcaemia). This causes tiredness, constipation, confusion, kidney stones and can affect the heart rhythm.

Primary hyperparathyroidism occurs in more than 90% of people with Multiple Endocrine Neoplasia syndrome Type 1, often starting in childhood or early adulthood.

What is a Pituitary adenoma?
The pituitary gland is a small pea-sized gland that sits underneath the brain, behind the bridge of your nose and on top of the optic nerves. Growths in the pituitary gland can become large (macroadenoma) but small growths (microadenoma) can still cause problems by secreting hormones.

Forty percent of people with Multiple Endocrine Neoplasia syndrome Type 1 develop a pituitary adenoma. The two most common pituitary growths in people with MEN1 are:

- Prolactin producing tumours, occurring in 20% and causing irregular periods, milk production in men and women and loss of sex drive
- Growth hormone producing tumours, occurring in 5 to 10% and causing acromegaly (or giantism if before puberty).

Ten percent of individuals diagnosed with a pituitary adenoma before age 40 have an MEN1 gene mutation.

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What is an Adrenocortical Tumour?
Adrenocortical tumours affect the outside layer of the adrenal gland (the adrenal cortex). They occur in 40% of people with Multiple Endocrine Neoplasia syndrome Type 1. Adrenocortical tumours secrete cortisol and aldosterone (resulting in primary hypercortisolism or hyperaldosteronism). They can become cancerous, although this is not common in people with MEN1.

Pheochromocytoma can occur but this is not common, affecting less than 1% of individuals with MEN1. Pheochromocytoma are much more commonly associated with genes such as VHL, NF1, the SDH genes and the TMEM127 and MAX genes. Follow the links on our website for more information on these genes and the hereditary cancer syndromes associated with them.

What is a Gastroduodenopancreatic neuroendocrine tumour GDP-NET?
Gastroduodenopancreatic neuroendocrine tumours (GDP NETs) are growths occurring in the glands found in the stomach, small intestine and pancreas. They are also known as GEP NETs (gastro-entero-pancreatic neuroendocrine tumours).

GDP NETs are usually named after the hormone they produce. Up to 70% of individuals with MEN1 develop one or more GDP NETs. The most common neuroendocrine tumours in Multiple Endocrine Neoplasia syndrome Type 1 are:

- Gastrinomas, which produce gastrin and increase stomach acid causing ulcers
- Insulinomas, which secrete insulin resulting in very low blood sugars (hypoglycaemia)
- Glucagonoma, which secrete glucagon, causing raised blood sugars and other problems

Neuroendocrine tumours can also occur in the thymus and affect 5% of people with MEN1. Thymic NETs are very often aggressive (grow rapidly and spread even when small).

Often, the thymic gland will be removed at the same time as surgery involving the thyroid or parathyroids in people with MEN1 (prophylactic thymectomy).

How is Multiple Endocrine Neoplasia syndrome Type 1 (MEN1) managed?
Management of MEN1 involves blood testing to detect increased levels of hormone levels and MRI scans to look for small growths in the endocrine glands.

This includes:

- annual blood tests from age 10
- MRI of the brain to look for growths affecting the pituitary gland. Often a once off at age 10 then every 2 years from age 20.
- MRI of the adrenal gland, pancreas, small bowel and chest (including the thymus) every 2 years from age 20.

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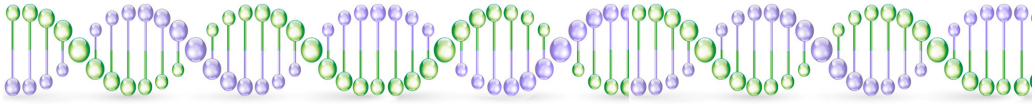

SYDNEY CANCER GENETICS

Is Multiple Endocrine Neoplasia syndrome Type 1 (MEN1) inherited?
Multiple Endocrine Neoplasia syndrome Type 1 is a hereditary cancer syndrome. 60% of individuals who meet the clinical diagnostic criteria for MEN1 carry a germline MEN1 mutation. This rises to 90% if there is close family member with an MEN1 type of tumour.

In addition to those people who meet the clinical criteria, testing for a heritable MEN1 mutation is recommended in anyone:

- with a neuroendocrine tumour affecting the thymus or bronchus, regardless of their age
- with more than one parathyroid tumour or a recurrence of a parathyroid tumour, regardless of their age
- who develops a parathyroid tumour (including both hyperplasia and adenoma) before age 40
- with more than one GDP-NET or a gastrinoma, regardless of their age
- who develops a neuroendocrine tumour involving the stomach, pancreas or small intestine before age 40

What are De Novo MEN1 mutations?
In individuals with MEN1, 10% of the time, they are the first person in their family to carry a MEN1 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.

There is a 50% chance of a person who carries a germline MEN1 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?
Has a neuroendocrine cancer, pituitary adenoma or hyperparathyroidism been detected in you or has a MEN1 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:

- Neuroendocrine Cancer Australia has details of support groups is for individuals and families affected by MEN1
- 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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