



Genetics Information Sheet

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IMPORTANT: Genetics Fact Sheets Number 1, 2, 3, 4, 5, **44** and the **relevant** support group listing from The 2004-2005 Genetics Resource Book should accompany this Information Sheet.



PO Box 317
St. Leonards NSW 1590



(02) 9926 7324



(02) 9906 7529



genetics@med.usyd.edu.au



www.genetics.com.au

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MULTIPLE ENDOCRINE NEOPLASIA, TYPE II; MEN2

Includes

MEN2A, MEN2B
medullary thyroid carcinoma with pheochromocytoma, Sipple syndrome, Familial Medullary Thyroid carcinoma

GENERAL INFORMATION ABOUT MEN2

Multiple Endocrine Neoplasia Type 2 or MEN2 is a rare inherited disorder where tumours develop in one or more of the endocrine glands, the thyroid, the adrenal and the parathyroid glands. Individuals with MEN2 have a high risk of developing a particular type of thyroid cancer known as medullary thyroid cancer or MTC.

Endocrine glands release hormones into the bloodstream. Hormones are powerful chemicals that travel through our blood to target organs and control their functioning. Normally hormones are carefully balanced to meet the body's needs. However people with MEN2 have an increased chance of developing tumours in the **thyroid, parathyroid and adrenal** endocrine glands which may lead to overproduction of some of the hormones produced by these glands.

There are three subtypes of MEN 2

- 1. MEN 2A:**
People with MEN 2A have a high risk of developing medullary thyroid cancer (MTC), pheochromocytoma (a tumour of the adrenal glands) and a parathyroid tumour. MEN2A is the most common type of MEN2 (60-90% of cases)
- 2. MEN 2B:**
People with MEN 2B have a high risk of medullary thyroid cancer (MTC) and an increased risk for pheochromocytoma. In addition they often have nerve tumours in their mouth and their gut, enlarged lips with a distinctive face, and a particular tall and thin appearance known as "Marfanoid" body shape.
- 3. Familial medullary thyroid carcinoma (FMTC):** People with FMTC have MTC without pheochromocytoma or parathyroid tumour.

MEN2 is inherited in an autosomal dominant manner which means that children of individuals with MEN2 have a 50% chance of inheriting the gene. Individuals with a family history of MEN2 even if they have no symptoms should seek genetic counselling and screening.

MORE INFORMATION ABOUT MEN2

The **thyroid gland** is found in the middle of the neck, just under the Adam's apple. Normally it makes the hormone thyroxine which regulates the metabolic rate. Thyroxine levels are **not** affected by Medullary Thyroid Cancer (MTC) in MEN2. The thyroid gland also makes the hormone **calcitonin** which has a small role in calcium metabolism. This hormone is made in the C cells of the thyroid. MTCs arise from the C cells and can make large amounts of calcitonin which can cause diarrhoea. There are no symptoms in early medullary thyroid cancer however when the tumour becomes large, a lump may appear in the neck and there may be lymph gland enlargement and diarrhoea.

The **adrenal glands** are small organs that are located above each of the kidneys. They release hormones such as **adrenaline** during stress. People with MEN2A & MEN2B may develop a rare tumour of the adrenal glands called a pheochromocytoma. This is mostly a benign (non-cancerous) tumour however pheochromocytoma results in adrenal hormones being made in excessive amounts. This can result in elevated blood pressure and symptoms such as anxiety, a racing pulse, palpitations, headache and flushing.

The **parathyroid glands** are 4 small glands in the neck behind the thyroid gland that release the parathyroid hormone which is involved with calcium metabolism. In MEN2A but not in MEN 2B, one or more parathyroid glands may become enlarged and overproduce parathyroid hormone resulting in the condition hyperparathyroidism. In hyperparathyroidism, the calcium in the blood becomes elevated and may lead to kidney stones, osteoporosis, abdominal pain, dehydration and general malaise.

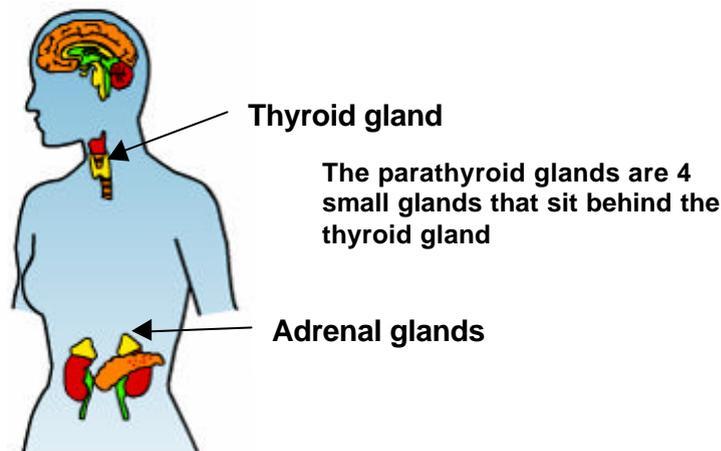


Diagram 1. Location of the thyroid, adrenal and parathyroid glands

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WHAT CAUSES MULTIPLE ENDOCRINE NEOPLASIA TYPE 2 (MEN 2)

MEN2 is a genetic disorder which is inherited in an autosomal dominant genetic manner. MEN2 results from having an alteration (a mutation) in a specific gene. This triggers tumour formation in some endocrine glands.

Autosomal dominant inheritance means most individuals with MEN2 inherit the gene from their mother or their father. Children of parents with MEN2, both boys and girls, each have a 50% chance of having the gene. This also means that they have a 50% chance of not having the gene. About 5% of cases of MEN2A and up to 50% cases of MEN2B arise “de-novo”, where there is no family history of MEN2 and the affected person is the first in the family.

For further information about the autosomal dominant form of genetic inheritance, see the Centre for Genetics Education Fact sheet 7 located on www.genetics.com.au.

The gene for MEN2 is known as the **RET gene**. Many mutations within the gene have been identified in individuals with MEN2. RET is an oncogene which promotes cell division and is located on chromosome 10 (10q11.2). MEN2 may occur when a mutation in the RET gene switches it on inappropriately resulting in uncontrolled cell growth.

For further information about the mechanism of oncogenes, see The Centre for Genetics Education Fact Sheet 44 on www.genetics.com.au.

Genetic testing is available for individuals in families suspected of having an inherited MEN2 gene. The search for a mutation is first done by taking blood from one of the affected family members. This testing may take time. If a mutation is identified in one member of the family affected by MEN2 then other blood relatives can be offered genetic testing to see if they have the mutation.

For more information about what genetic counselling can offer, please refer to Genetics Fact Sheet # 5.

Multiple Endocrine Neoplasia 1(MEN1).

A condition called MEN1 exists that is also a dominantly inherited genetic disorder of the endocrine glands. MEN1 however is characterised by tumours in the parathyroid gland, the pituitary and the pancreas, is the result of mutations in the MEN1 gene. It is distinctly different from MEN2.

WHO IS AFFECTED BY MULTIPLE ENDOCRINE NEOPLASIA TYPE 2 (MEN 2)?

MEN2 is a dominantly inherited genetic disorder affecting males and females in equal numbers. It is very rare.

The age when symptoms first appear is typically in early childhood in MEN2B, late childhood or early adulthood in MEN2A, and in adulthood in FMTC.

IS THERE ANY TREATMENT FOR MULTIPLE ENDOCRINE NEOPLASIA TYPE 2 (MEN 2)?

Management of people with MEN2 is aimed at prevention and early detection of tumours as well as control of effects from altered hormone levels. Medullary thyroid cancer may spread to lymph nodes if not treated. Serious complications may also arise from the presence of pheochromocytoma and parathyroid tumours.

Surgical removal of the thyroid gland as a preventative measure is recommended treatment. For children the age for surgery differs according to the type of mutation that has occurred. Generally surgery is recommended from an early age and for individuals with MEN2B, as early as possible. The function of the gland can be replaced by giving the hormone thyroxine. The hormone calcitonin does not need to be replaced.

Screening for the presence of pheochromocytoma and hyperparathyroidism is also conducted before thyroid surgery and adrenal or parathyroid surgery may also be appropriate. Annual tests of the blood and possibly the urine for screening with follow up are recommended.

RESOURCES

To find out whether there is a relevant Australian Support Group for general peer support and possible contact with other affected individuals or families, contact:

Association of Genetic Support of Australasia (AGSA)

66 Albion Street

SURRY HILLS NSW 2010

☎ (02) 9211 1462

E-mail: agsa@ozemail.com.au

Web: <http://www.agsa-geneticsupport.com.au>

Additional information and Support may be available from the following international sources:

OVERSEAS GROUPS

The Association for Multiple Endocrine Neoplasia Disorders (AMEND)

Website provides a link and resource for patients throughout the world who have the rare hereditary conditions of M.E.N. Type 1 or Type 2.

<http://www.amend.org.uk/website>

For information regarding local genetic counselling services:

The Centre for Genetics Education

PO Box 317

ST LEONARDS NSW 1590

☎ (02) 9926 7324

E-mail: genetics@med.usyd.edu.au

Web: <http://www.genetics.com.au>

REFERENCES

This information sheet is based on information obtained from the follow sources:

OMIM MENDELIAN INHERITANCE IN MAN ON-LINE:

<http://www.ncbi.nlm.nih.gov/Omim>

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In consultation with key researchers and clinical experts.