Genetics Information Sheet

If this Information Sheet is more than 6 months old (date of production at foot of document), please contact The Centre for Genetics Education for an update.

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

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MULTIPLE ENDOCRINE NEOPLASIA, TYPE 1

ALSO KNOWN AS

- MEN1
- Familial Multiple Endocrine Neoplasia, Type 1 (FMEN1)
- Endocrine adenomastosis, multiple
- MEA1
- Wermer syndrome

GENERAL INFORMATION ABOUT MULTIPLE ENDOCRINE NEOPLASIA TYPE 1

Multiple endocrine neoplasia type 1 (MEN1) is a rare inherited disorder characterised by a high frequency of peptic ulcer disease and abnormalities involving the endocrine glands: the pituitary, parathyroid, and pancreas. Endocrine glands are responsible for releasing hormones into the bloodstream. Hormones are powerful chemicals that travel through the blood to target organs, and control their functioning.

Normally, hormones released by endocrine glands are carefully balanced to meet the body's needs. However, people with a faulty MEN1 gene have an increased chance of developing overactivity and enlargement of these endocrine glands. They also have an increased chance of developing tumours in these glands, which can sometimes become malignant (cancerous).

Peptic ulcer disease may occur because the pancreas releases excessive amounts of the hormone gastrin (the hormone which governs the production of acid for digestion).

This disease varies considerably between different families, but amongst members of the same family it can

be very similar. For example, there may be a high frequency of severe peptic ulcer disease amongst members of one family, but in another family no members have peptic ulcer disease.

SYMPTOMS OF MULTIPLE ENDOCRINE NEOPLASIA TYPE 1

MEN1 can lead to overactivity and enlargement of certain endocrine glands. The endocrine system is a network of glands and other organs which secrete or produce hormones into the bloodstream. These hormones control many body functions such as metabolism and growth. The glands of the endocrine system include the thyroid, the pituitary, the pancreas and the gonads (testes and ovaries) but those most commonly affected by Multiple Endocrine Neoplasia are the parathyroid, pituitary and pancreas.

Abnormalities of the endocrine system can lead to the formation of neoplasms or tumours which may be either benign or malignant (cancerous). Although not cancerous, benign tumours can disrupt normal function by obstructing nearby important tissues. Tumours have been reported in the lungs, pancreas, pituitary and adrenal glands, ovaries and the thymus.

The **parathyroid glands** are the most frequently affected glands in MEN1. There are four of these in the body, located near the thyroid gland. Their function is to maintain a normal supply of calcium in the blood, bones and urine. When they are overactive, this can lead to increased levels of calcium in the urine, resulting in kidney stones or kidney damage. Symptoms of excessive parathyroid hormone production include tiredness, weakness, muscle or bone pain, constipation, indigestion, kidney stones or the thinning of bones. Hyperparathyroidism may cause osteoporosis.

The **pancreas gland** is responsible for the release of digestive juices into the intestines. When excessive amounts of the hormone gastrin (the hormone which governs the production of acid for digestion) are produced, intractable peptic ulcer with accompanying ulcerative gastritis, epigastric pain and diarrohea will result.

The **pituitary gland** located in the head is a very important gland responsible for the production of many hormones. These include prolactin which controls breast milk production and influences fertility; and growth hormone which regulates body growth. Some of the rarer complications of MEN1 arise from tumours located in the pituitary gland.

There is considerable variation in the degree of severity in this disorder, even among members of the same family, although the involvement of particular glands seems to cluster in families.

In many cases, people with MEN1 have no symptoms, and are only diagnosed after routine biochemical investigations or blood tests.

WHAT CAUSES MULTIPLE ENDOCRINE NEOPLASIA?

Multiple Endocrine Neoplasia 1 (MEN1) is a genetic disorder which is inherited in an autosomal dominant genetic manner. An individual may inherit a fault in the MEN1 gene (a tumour suppressor gene) which predisposes them to developing the disease. Symptoms will only appear if a second copy of the gene also becomes

faulty at some stage of their life. When an individual has a mutation in the MEN1 gene, the chances of passing this change or mutation on to children is 1 in 2 or 50%. Individuals with a family history of MEN1 (even if they have had no symptoms) should receive genetic counselling and screening for MEN1 inheritance.

For further information about genes, chromosomes, genetic disorders and the autosomal dominant form of genetic inheritance, see Genetic Fact Sheets 1,3 and 5.

The gene for MEN1 is on the long arm of chromosome 11 in the region known as 11q13. Around 50 mutations or alterations within the gene have been identified. However, about 10% of cases have arisen spontaneously ie. there has not been a family history and the affected person is the first person in the family with the condition.

The function of the gene responsible for MEN1 is one of tumour suppression. For further explanation about the mechanism of this gene, see Genetics Fact Sheet # 29.

WHO IS AFFECTED BY MULTIPLE ENDOCRINE NEOPLASIA TYPE 1?

Multiple Endocrine Neoplasia is a dominantly inherited genetic disorder affecting males and females in equal numbers. It is very rare and occurs at a rate of between 0.02-0.2 per 10,000 of the population.

The age at which symptoms first appear varies. Most gene carriers will develop problems in their endocrine glands by 30 years of age, but some have no symptoms until advanced age.

IS THERE ANY TREATMENT FOR MUTIPLE ENDOCRINE NEOPLASIATYPE 1?

Management of people with MEN 1 is aimed at prevention and early detection of tumours as well as control of effects from excessively high hormone levels. Screening protocols may include: fasting blood tests to check calcium and hormone levels, abdominal ultrasound, magnetic resonance imaging of the pituitary gland, CT scan of abdomen, bone mineral density studies. Surgical options depend on which glands are involved in the disease. If a gland is surgically removed, the patient must be given medication to replace the hormones that gland produced. Careful monitoring by an endocrinologist (medical specialist in the area of hormones) is recommended.

Periodic screening of first- degree relatives (parents, brothers, sister, children) of affected individuals is recommended. Quite often symptoms do not appear until well into adult life. However, once and individual has reached 50 years of age without symptoms, he or she is unlikely to have inherited the MEN1 gene.

Genetic counselling is also recommended for affected individuals and their families. For more information about what genetic counselling can offer, please refer to Genetics Fact Sheet # 5.

RESOURCES

There is no official support group for this disorder but further information may be available from:

The Australian Pituitary Foundation
PO Box 327
ALLAWAH NSW 2218
Tel: 02 9580 6050

General peer support and possible contact with other affected individuals or families may be available from:

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:

NIH/National Institute of Child Health and Human Development
NICHHD Information Resource Centre
PO Box 3006
Rockville, MD 20847
Tel: 1-800-370-2943 or 301 496 5133

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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