Multiple endocrine neoplasia, type 2 (MEN2) is caused by pathogenic (or harmful) variants in the *RET* gene. Individuals with MEN2 are at an increased risk to develop medullary thyroid cancer, pheochromocytomas of the adrenal glands (rare tumor that can make your adrenal glands produce more hormone than they're supposed to), and parathyroid gland adenomas (benign tumors). MEN2 can be broken down into three subtypes:

- Multiple Endocrine Neoplasia, type 2A
- Multiple Endocrine Neoplasia, type 2B, and
- Familial Medullary Thyroid Carcinoma (FMTC)

All three subtypes have a 95-100% chance to develop MTC. Individuals with MEN2A and MEN2B also have a 50% chance to develop pheochromocytoma, while people with MEN2A also have a 20-30% chance to develop parathyroid disease.

Subtype	Medullary thyroid cancer	Pheochromocytoma	Parathyroid disease
MEN2A	95%	50%	20-30%
MEN2B	100%	50%	uncommon
FMTC	100%	0%	0%

Pathogenic variants in RET are inherited in an autosomal dominant pattern, meaning that children of someone who carries a pathogenic variant each have a 50% risk to inherit the variant and associated cancer risks. Notably, women and men both have the RET gene and have the same chances to inherit and pass down variants in this gene. Therefore, both sides of the family are important when assessing inherited risk. However, the associated cancers and lifetime risks are different between men and women.

How is Multiple Endocrine Neoplasia, type 2 diagnosed?

A diagnosis of MEN2 is made if your personal or family history meets established clinical criteria (based on medical history, physical examination, and family history) that has been evaluated by a provider who is familiar with MEN2. Some red flags in a family history that can increase the chance for MEN2 are:

- MEN2A: should be suspected in anyone with one or more specific endocrine tumors (medullary thyroid cancer, pheochromocytoma, or parathyroid adenoma/hyperplasia)
- MEN2B: should be suspected in anyone with distinctive facial features (masses called neuromas around the lip and tongue, differences in the nerve fibers in the cornea of the eye, long limbs, high arches of the foot, overly flexible, etc)

- FMTC: should be suspected in families with more than one individual who has been diagnosed with medullary thyroid cancer, but also with an absence of parathyroid adenomas/hyperplasia and pheochromocytomas

Genetic Testing for Multiple Endocrine Neoplasia, type 2

Genetic testing for pathogenic variants in the *RET* gene is currently available, but there are a few ways to approach testing:

- *Single site analysis*: Testing specific to a known pathogenic variant in the family
- *Full gene sequencing and rearrangement analysis*: Comprehensive testing to search for all currently detectable pathogenic variants in the genes.
- *Gene panels*: Newer, more broadly based gene tests that would include not only the RET gene, but other genes known or suspected to be associated with increased cancer risks

Cancer Screening and Risk Management for Multiple Endocrine Neoplasia, type 2

Management for individuals with MEN2 is complex and largely individualized depending on the person's medical and family history, as well as the specific gene change that they carry. Sometimes the specific pathogenic variant can tell us whether someone has MEN2A, MEN2B, or FMTC. The specific variant can also tell us how high someone's risk may be to develop related health concerns, and what age to begin certain types of screening. There may also be specific medications that your doctor may have you avoid if you have a diagnosis of MEN2. Preventative surgery, lab testing, and imaging with ultrasound, MRI, or CT scan can be used to help keep individuals who have MEN2 healthy. It is important to work with your doctor to develop the screening plan that will work best for you.

Click here to learn more about scheduling a genetic counseling appointment for questions about hereditary cancer predisposition.

Additional Resources

American Multiple Endocrine Neoplasia Support (AMENSupport)