UT Southwestern Harold C. Simmons Comprehensive Cancer Center | NCI Designated Comprehensive Cancer Center

Multiple Endocrine Neoplasia Type 2 (MEN2)

What You Should Know About Multiple Endocrine Neoplasia Type 2 (MEN2)

MEN2 is a condition caused by mutations in the *RET* gene. MEN2 is classified into three subtypes: MEN2A, FMTC (Familial Medullary Thyroid Cancer), and MEN2B. In all subtypes, there is a very high risk of developing medullary thyroid cancer (MTC). In addition, some individuals with MEN2 have an increased risk for tumors in the adrenal gland (pheochromocytoma) and parathyroid glands. The features and cancer risks vary by specific *RET* mutation.

Cancer/Tumor Risks Associated with Multiple Endocrine Neoplasia Type 2 (MEN2)

- Medullary Thyroid Cancer: Individuals with MEN2 have a 95-100% risk to develop medullary thyroid cancer. This can occur as early as infancy or childhood. Risks can also vary based on the mutation.
- Pheochromocytoma: Individuals with MEN2 have up to a 50% lifetime risk to develop a pheochromocytoma. This risk varies by MEN2 subtype. These tumors are typically not cancerous, but can produce excessive amounts of hormones called catecholamines, which can cause very high blood pressure. Parathyroid Tumors: Individuals with MEN2 have up to a 25% lifetime risk to develop parathyroid tumors. This risk varies by MEN2 subtype. These tumors are typically not cancerous, but they can produce excessive amounts of parathyroid hormone (hyperparathyroidism). This causes calcium to be moved from the bone to the blood, which causes the bones to become weak, and can cause kidney stones to develop. Cutaneous lichen amyloidosis: Rarely, individuals with MEN2 have been reported to develop cutaneous lichen amyloidosis. This skin condition presents with lesions, particularly on the back and scapular area that improves with sun exposure and worsens with stress. These lesions can present at an early age.

Risks to Family Members

MEN2 is inherited in an autosomal dominant fashion. This means that children, brothers, sisters, and parents of individuals with a *RET* mutation have a 1 in 2 (50%) chance of having the mutation as well. Some individuals (approximately 50%) with MEN2B have a new *RET* mutation which was not inherited from either parent, also known as a "de novo" mutation. Individuals with a *RET* mutation may develop thyroid cancer, tumors in the adrenal gland, tumors in the parathyroid glands, or none of the above. Both males and females can inherit a familial *RET* mutation and can pass that it on to their children.

Managing Cancer Risks

- Medullary Thyroid Cancer: Annual physical examination, thyroid ultrasounds, and serum calcitonin levels beginning at age 3-5 years, or at the time of MEN2 diagnosis. Prophylactic thyroidectomy (surgical removal of the thyroid gland) should be considered for individuals with an elevated serum calcitonin levels for moderate risk mutation carriers. The recommended age to initiate screening and/or consider thyroidectomy varies based on the specific *RET* gene mutation.
- Pheochromocytoma: Annual measurement of plasma or 24 hour-urinary fractionated metanephrines beginning at age 11-16, or at the time of MEN2 diagnosis. The recommended age to initiate surveillance varies based on the specific *RET* gene mutation. MRI and/or CT should be performed with biochemical evidence or symptoms consistent with a pheochromocytoma. If a pheochromocytoma is identified, surgery to remove all or part of the affected adrenal gland(s) is recommended.
- Hyperparathyroidism: Annual biochemical screening of albumin-corrected calcium or ionized serum calcium measurements beginning at age 11-16, or at the time of MEN2 diagnosis. The recommended age to initiate

surveillance varies based on the specific *RET* gene mutation. Visibly enlarged parathyroid glands should be surgically removed.

- Cutaneous lichen amyloidosis: Consideration of a dermatological exam can be given.

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