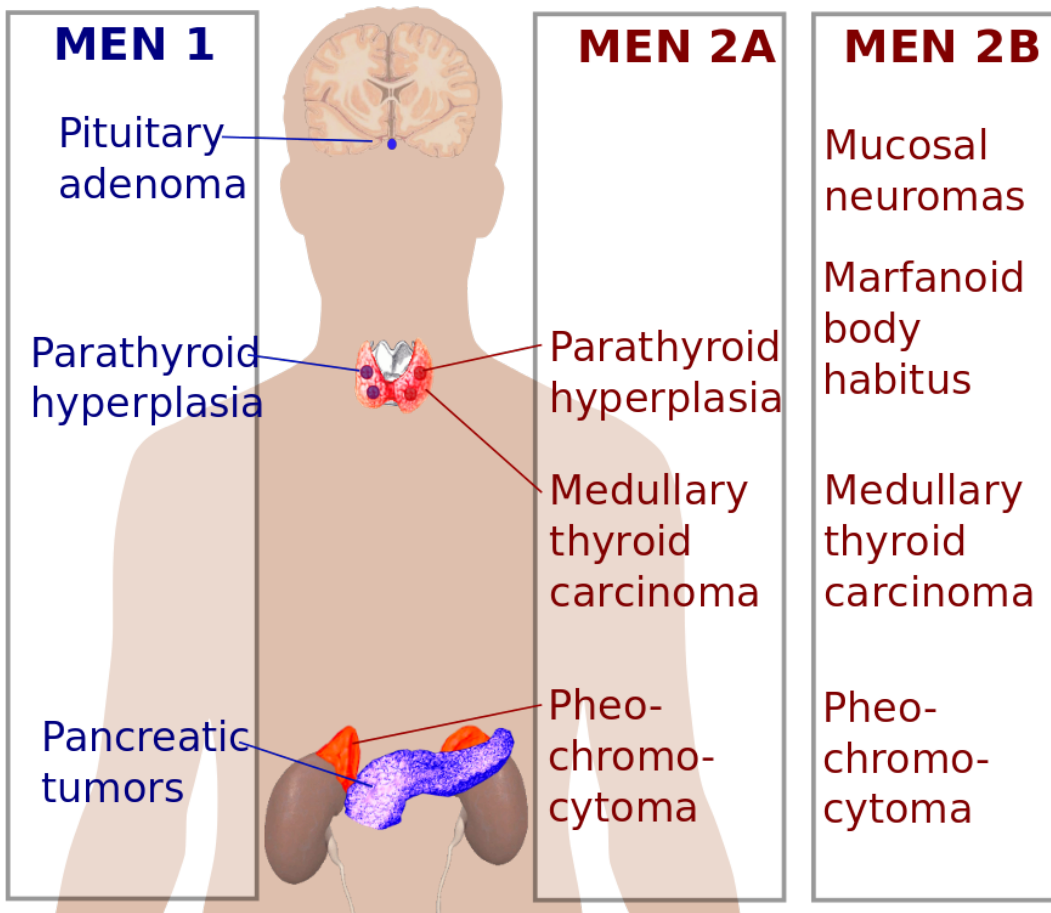


Multiple Endocrine Neoplasia (MEN) — Symptoms

[See online here](#)

The multiple endocrine syndromes are inherited autosomal dominantly and consist of two superior groups (I and II). The second group can be further divided into three subgroups (IIa, IIb and FMTC-only). The respective upper groups have different causes on molecular genetic level. Characteristic signature diseases i.a. appear as part of these syndromes.



MEN-1 Syndrome (Wermer Syndrome)

MEN-1 syndrome belongs to the multiple endocrine syndromes and is inherited in an autosomal dominant manner.

Etiology of MEN-1 syndrome

The cause of MEN-1 syndrome is a mutation of the **menin gene**. This gene is located on the long arm of **chromosome 11** (11q13).

The menin gene is a **tumor suppressor gene**. Proteins that regulate the cell cycle as well as apoptosis, belong to this group. The risk of neoplasias is increased due to the mutation of a tumor suppressor gene.

Note: MEN-1 syndrome is caused by a mutation of the menin gene.

Diseases of MEN-1 syndrome

The signature disease of MEN-1 syndrome is **primary hyperparathyroidism** (95% of cases). Here, an increased level of parathormone occurs due to parathyroid hyperfunction.

Note: The signature disease of MEN-1 syndrome is primary hyperparathyroidism.

Tumors of MEN-1 syndrome

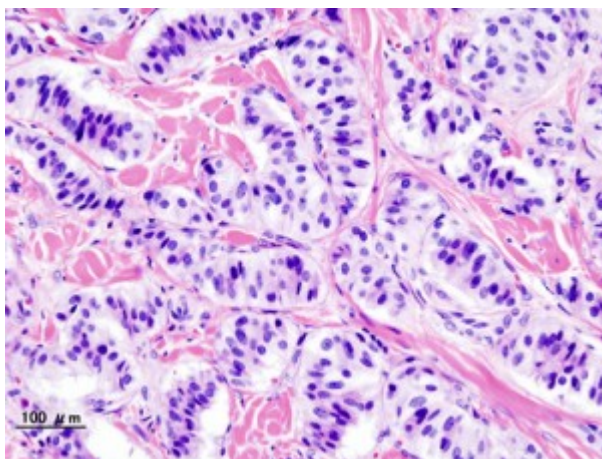
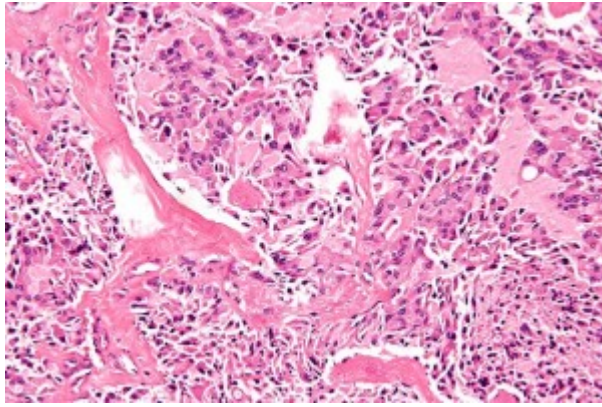


Image: Histopathology of a pancreatic endocrine tumor (insulinoma). By KGH, License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

The possible tumors that can evolve from a MEN-1 syndrome are tumors of the pancreas like gastrinoma and insulinoma. These 2 tumors belong to the spectrum of **endocrine pancreatic tumors** and appear in 50% of the cases. Tumors of the **hypophysis** are rarer (about 30–50% of the cases) but are still common in MEN-1 syndrome.

MEN-2 Syndrome

MEN-2 syndrome also displays an **autosomal dominant** inheritance pattern and can further be divided into **Sipple syndrome** (2a), **Gorlin syndrome** (2b), and **FMTC-only** (familial medullary thyroid carcinoma).



[Image](#): Medullary thyroid carcinoma. By Nephron, License: [CC BY-SA 3.0](#)

FMTC-only is a special form of MEN-2 syndrome since only **medullary thyroid carcinomas** appear. That is why it is also called a **non-MEN syndrome** because no multiple endocrine tumors are present.

Etiology of MEN-2 syndrome

The etiology of the 3 subgroups of MEN-2 syndrome is identical. All 3 are caused by a mutation of the **Ret-proto-oncogene** that codes for a transmembranous tyrosine kinase. The locus of the mutation is on the long arm of **chromosome 10** (10q11.2).

Clinical presentation of MEN-2a syndrome (Sipple syndrome)

Sipple syndrome, comprising 70% of MEN-2 cases, is notably more common than Gorlin syndrome (about 10% of all cases).

Diseases of MEN-2a syndrome

Phaeochromocytoma (approx. 50% of cases) and **primary hyperparathyroidism** (20% of cases) occur as a part of Sipple syndrome.

Note: Primary hyperparathyroidism can be part of MEN-1 syndrome and MEN-2a syndrome.

Tumors of MEN-2a syndrome

The most common tumor and signature disease of MEN-2a syndrome is **medullary thyroid carcinoma (C cell carcinoma)**. This occurs in almost 100% of the cases.

Note: The signature disease of Sipple syndrome is medullary thyroid carcinoma.

Clinical presentation of MEN-2b syndrome (Gorlin syndrome)

Gorlin syndrome is the least often occurring subgroup of MEN-2 syndrome, accounting for 10% of the cases. In about 60% of the cases, Gorlin syndrome evolves as part of a new mutation, which means that it is not inherited in an autosomal dominant fashion. These cases are called **sporadic cases**.

Diseases of MEN-2b syndrome

Similar to Sipple syndrome, a phaeochromocytoma also occurs in 50% of Gorlin syndrome

cases.

Note: In contrast, primary hyperparathyroidism does not occur in Gorlin syndrome. Other clinical characteristics that appear as a part of Gorlin syndrome, are **mucosal neurinomas, ganglioneuromatoses** in organs like the tongue or intestine, as well as **marfanoid habitus**. Characteristics of marfanoid habitus are a lean, tall body shape with long extremities and hyperextension of joints.

Tumors of MEN-2b syndrome

Similar to Sipple syndrome, **medullary thyroid carcinoma** is also the signature disease of Gorlin syndrome (about 100% of the cases).

Clinical presentation of FMTC-only syndrome (non-MEN syndrome)

As mentioned above, an FMTC-only syndrome is a special form as only **medullary thyroid carcinomas** occur.

Note: Always think of a MEN-2 syndrome as comprising familial medullary thyroid carcinomas. With a molecular genetic diagnosis, 'unaffected' family members can also be tested for the mutation so a prophylactic thyroidectomy can be considered.

References

Brewer, J. J. (2014). Multiple Endocrine Neoplasia (MEN) Syndromes. *Surgical Oncology*, 573-584. doi:10.1007/978-1-4939-1423-4_25

Koch, C. A. (2004). Multiple Endocrine Neoplasia (MEN) Type 2. *Encyclopedia of Endocrine Diseases*, 278-282. doi:10.1016/b0-12-475570-4/00887-8

Multiple Endocrine Neoplasia (MEN) Syndrome. (n.d.). *Encyclopedia of Diagnostic Imaging*, 1168-1168. doi:10.1007/978-3-540-35280-8_1619

Vrkljan, Milan, Doko, Marko, Bekić, Marijo, ... Mladen. (2001). *Multiple Endocrine Neoplasia: Case Report*. SestreMilosrdnice University hospital and Institute of Clinical Medical Research.

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