

## Multiple Endocrine Neoplasia Type 1

Multiple endocrine neoplasia type 1 (MEN1) is a hereditary syndrome caused by pathogenic variants in the *MEN1* gene and is associated with a combination of endocrine and nonendocrine tumors. In MEN1, tumors are most often found in the parathyroid gland, islet cells of the pancreas, and pituitary gland. Tumors can also form in other endocrine glands and the digestive tract. The majority of MEN1 tumors are benign but tumors of the gastroenteropancreatic tract and thymic carcinoids may be malignant. Endocrine tumors cause an increased hormone production based on tumor type, resulting in a wide range of symptoms.

### Disease Overview

#### Incidence

1/30,000<sup>1,2</sup>

#### Symptoms

- MEN1 can include development of multiple endocrine and nonendocrine tumors<sup>3</sup>
- Common endocrine tumors:
  - Parathyroid
  - Gastroenteropancreatic tract (gastrinoma, insulinoma, glucagonoma, pancreatic islet cell tumor)
  - Pituitary (prolactinoma)
  - Gastrinoma
  - Carcinoid (thymic, bronchial, gastric)
  - Adrenal
  - Medullary carcinoma of the thyroid
- Nonendocrine tumors:
  - Facial angiofibromas
  - Collagenomas
  - Lipomas
  - Meningiomas
  - Ependymomas
  - Leiomyomas

### Genetics

#### Gene

*MEN1*

#### Inheritance

Autosomal dominant

#### Penetrance

Variable<sup>4,5,6</sup>

### Tests to Consider

#### [Multiple Endocrine Neoplasia Type 1 \(MEN1\) Sequencing and Deletion/Duplication 2005360](#)

**Method:** Polymerase Chain Reaction/Sequencing/Multiplex Ligation-dependent Probe Amplification

Preferred initial test to confirm diagnosis of MEN1

#### [Multiple Endocrine Neoplasia Type 1 \(MEN1\) Sequencing 2005359](#)

**Method:** Polymerase Chain Reaction/Sequencing

Acceptable initial test to confirm diagnosis of MEN1

#### [Familial Mutation, Targeted Sequencing 2001961](#)

**Method:** Polymerase Chain Reaction/Sequencing

Useful when a pathogenic familial variant identifiable by sequencing is known

#### [Deletion/Duplication Analysis by MLPA 3003144](#)

**Method:** Multiplex Ligation-dependent Probe Amplification

Use to assess for large deletion/duplication previously identified in a family member

See [Related Tests](#) for tumor testing and screening including anterior pituitary and carcinoid tumor testing, gastrinoma testing, medullary thyroid carcinoma testing, pancreatic neuroendocrine tumor testing, parathyroid tumor testing, and pheochromocytoma testing.



- ~50% by 20 years
- >95% by 40 years

De novo variants: ~10%

## Variants

Inactivating variants of *MEN1* tumor suppressor gene

## Test Interpretation

### Clinical Sensitivity

Combined testing: ~94%

- Sequencing: 90%<sup>3</sup>
- Deletion/duplication: 4%<sup>3</sup>

### Results

- Positive:
  - One pathogenic variant detected in *MEN1*
  - Confirms diagnosis and etiology of MEN1
- Negative:
  - No detectable pathogenic variant detected in *MEN1*
  - Reduces, but does not exclude, a diagnosis of MEN1
- Uncertain: variants of unknown clinical significance may be detected

### Limitations

- Not evaluated:
  - Regulatory region or deep intronic variants
  - Breakpoints of large deletions/duplications
  - Variants in genes other than *MEN1*
- Diagnostic errors can occur due to rare sequence variations

### References

1. Brandi ML. [Rare Disease Database: multiple endocrine neoplasia type 1](#). National Organization for Rare Disorders. [Published: 2018; Accessed: Sep 2019]
2. Ki Wong F, Burgess J, Nordenskjöld M, et al. [Multiple endocrine neoplasia type 1](#). *Semin Cancer Biol*. 2000;10(4):299-312. PubMed
3. Giusti F, Marini F, Brandi ML. [Multiple endocrine neoplasia type 1](#). In: Adam MP, Ardinger HH, Pagon RA, et al, editors. *GeneReviews*, University of Washington; 1993-2021. [Last update: Dec 2017; Accessed: Feb 2020]
4. Online Mendelian Inheritance in Man. [Multiple endocrine neoplasia type 1](#). [Edited: Feb 2017; Accessed: Mar 2020]
5. Bassett JH, Forbes SA, Pannett AA, et al. [Characterization of mutations in patients with multiple endocrine neoplasia type 1](#). *Am J Hum Genet*. 1998;62(2):232-244. PubMed
6. Carroll RW. [Multiple endocrine neoplasia type 1 \(MEN1\)](#). *Asia Pac J Clin Oncol*. 2013;9(4):297-309. PubMed

### Additional Resources

Thakker RV, Newey PJ, Walls GV, et al. [Clinical practice guidelines for multiple endocrine neoplasia type 1 \(MEN1\)](#). *J Clin Endocrinol Metab*. 2012;97(9):2990-3011. PubMed



## Related Information

[Multiple Endocrine Neoplasias - MEN](#)

## Related Tests

[Somatostatin Quantitative, Plasma 2010001](#)

**Method:** Quantitative Extraction/Immunoassay

[Metanephrines Fractionated by HPLC-MS/MS, Urine 2007996](#)

**Method:** Quantitative High Performance Liquid Chromatography-Tandem Mass Spectrometry

[Insulin-Like Growth Factor 1 \(IGF-1\) with Calculated Z-Score 2007698](#)

**Method:** Quantitative Chemiluminescent Immunoassay

[Thyroid Stimulating Hormone with reflex to Free Thyroxine 2006108](#)

**Method:** Quantitative Electrochemiluminescent Immunoassay

[Pancreatic Polypeptide 0099436](#)

**Method:** Quantitative Radioimmunoassay

[Vasoactive Intestinal Peptide 0099435](#)

**Method:** Quantitative Radioimmunoassay

[Glucagon 0099165](#)

**Method:** Quantitative Radioimmunoassay

[Chromogranin A, Serum 3002867](#)

**Method:** Immunofluorescence

[5-Hydroxyindoleacetic Acid \(HIAA\), Urine 0080420](#)

**Method:** Quantitative High Performance Liquid Chromatography - Tandem Mass Spectrometry

[Serotonin, Whole Blood 0080395](#)

**Method:** Quantitative High Performance Liquid Chromatography

[Proinsulin, Intact/Insulin Ratio 0070256](#)

**Method:** Quantitative Chemiluminescent Immunoassay/Quantitative Chemiluminescent Immunoassay

[Parathyroid Hormone, Intact with Calcium 0070172](#)

**Method:** Quantitative Electrochemiluminescent Immunoassay

[Prolactin 0070115](#)

**Method:** Quantitative Chemiluminescent Immunoassay

[C-Peptide, Serum or Plasma 0070103](#)

**Method:** Quantitative Chemiluminescent Immunoassay

[Gastrin 0070075](#)

**Method:** Quantitative Chemiluminescent Immunoassay

[Adrenocorticotrophic Hormone 0070010](#)

**Method:** Quantitative Electrochemiluminescent Immunoassay (ECLIA)

[Calcitonin 0070006](#)

**Method:** Quantitative Chemiluminescent Immunoassay

[Metanephrines, Plasma \(Free\) 0050184](#)



**Method:** Quantitative Liquid Chromatography-Tandem Mass Spectrometry

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