TABLE 408-1 MULTIPLE ENDOCRINE NEOPLASIA (MEN) SYNDROMES

Type (Chromosomal Location)	Tumors (Estimated Penetrance)	Gene and Most Frequently Mutated Codons
MEN 1 (11q13)	Parathyroid adenoma (90%)	*MEN1*
	Enteropancreatic tumor (30–70%)	83/84, 4-bp del (≈4%)
	• Gastrinoma (>50%)	119, 3-bp del (≈3%)
	• Insulinoma (10–30%)	209-211, 4-bp del (≈8%)
	• Nonfunctioning and PPoma (20–55%)	418, 3-bp del (≈4%)
	• Glucagonoma (<3%)	514-516, del or ins (≈7%)
	• VIPoma (<1%)	Intron 4 ss (≈10%)
	Pituitary adenoma (15–50%)	
	• Prolactinoma (60%)	
	• Somatotrophinoma (25%)	
	• Corticotropinoma (<5%)	
	• Nonfunctioning (<5%)	
	Associated tumors	
	• Adrenal cortical tumor (20–70%)	
	• Pheochromocytoma (<1%)	
	• Bronchopulmonary NET (2%)	
	• Thymic NET (2%)	
	• Gastric NET (10%)	
	• Lipomas (>33%)	
	• Angiofibromas (85%)	
	• Collagenomas (70%)	
	• Meningiomas (8%)	
MEN 2 (10 cen-10q11.2)		
MEN 2A	MTC (90%)	*RET*
	Pheochromocytoma (>50%)	634, e.g., Cys → Arg (~85%)
	Parathyroid adenoma (10–25%)	
MTC only	MTC (100%)	*RET* 618, missense (>50%)
MEN 2B (also known as MEN 3)	MTC (>90%)	*RET* 918, Met → Thr (>95%)
	Pheochromocytoma (>50%)	
	Associated abnormalities (40–50%)	
	• Mucosal neuromas	
	• Marfanoid habitus	
	• Medullated corneal nerve fibers	
	• Megacolon	
MEN 4 (12p13)	Parathyroid adenoma[a]	*CDKN1B*; no common mutations identified to date
	Pituitary adenoma[a]	
	Reproductive organ tumors[a] (e.g., testicular cancer, neuroendocrine cervical carcinoma)	
	?Adrenal + renal tumors[a]	

[a]Insufficient numbers reported to provide prevalence information.

Note: Autosomal dominant inheritance of the MEN syndromes has been established.

Abbreviations: del, deletion; ins, insertion; MTC, medullary thyroid cancer; NET, neuroendocrine tumor; PPoma, pancreatic polypeptide–secreting tumor; VIPoma, vasoactive intestinal polypeptide–secreting tumor.

Source: Reproduced from RV Thakker et al: J Clin Endocrinol Metab 97:2990, 2012.

the calcium-sensing receptor, have been used to treat primary hyperparathyroidism in some patients when surgery is unsuccessful or contraindicated.

Pancreatic Tumors (See also Chap. 113) The incidence of pancreatic islet cell tumors, which are NETs, in patients with MEN 1 ranges from 30 to 80% in different series. Most of these tumors (Table 408-1) produce excessive amounts of hormone (e.g., gastrin, insulin, glucagon, vasoactive intestinal polypeptide [VIP]) and are associated with distinct clinical syndromes, although some are nonfunctioning or nonsecretory. These pancreatic islet cell tumors have an earlier age at onset in patients with MEN 1 than in patients without MEN 1.

Gastrinoma Gastrin-secreting tumors (gastrinomas) are associated with marked gastric acid production and recurrent peptic ulcerations, a combination referred to as the Zollinger-Ellison syndrome. Gastrinomas occur more often in patients with MEN 1 who are older than age 30 years. Recurrent severe multiple peptic ulcers, which may perforate, and cachexia are major contributors to the high mortality. Patients with Zollinger-Ellison syndrome may also suffer from diarrhea and steatorrhea. The diagnosis is established by demonstration of an elevated fasting serum gastrin concentration in association with increased basal gastric acid secretion (Table 408-3). However, the diagnosis of Zollinger-Ellison syndrome may be difficult in hypercalcemic MEN 1 patients, because hypercalcemia can also cause hypergastrinemia.