TABLE 113-2 GASTROINTESTINAL NEUROENDOCRINE TUMOR SYNDROMES

Name	Biologically Active Peptide(s) Secreted	Incidence (New Cases/10^6 Population/ Year)	Tumor Location	Malignant, %	Associated with MEN 1, %	Main Symptoms/Signs
I. Established Specific Functional Syndromes						
A. Carcinoid syndrome due to GI-NET						
Carcinoid syndrome	Serotonin, possibly tachykinins, motilin, prostaglandins	0.5–2	Midgut (75–87%) Foregut (2–33%) Hindgut (1–8%) Unknown (2–15%)	95–100	Rare	Diarrhea (32–84%) Flushing (63–75%) Pain (10–34%) Asthma (4–18%) Heart disease (11–41%)
B. Well-established functional pNET syndromes						
Zollinger-Ellison syndrome	Gastrin	0.5–1.5	Duodenum (70%) Pancreas (25%) Other sites (5%)	60–90	20–25	Pain (79–100%) Diarrhea (30–75%) Esophageal symptoms (31–56%)
Insulinoma	Insulin	1–2	Pancreas (>99%)	<10	4–5	Hypoglycemic symptoms (100%)
VIPoma (Verner-Morrison syndrome, pancreatic cholera, WDHA)	Vasoactive intestinal peptide	0.05–0.2	Pancreas (90%, adult) Other (10%, neural, adrenal, periganglionic)	40–70	6	Diarrhea (90–100%) Hypokalemia (80–100%) Dehydration (83%)
Glucagonoma	Glucagon	0.01–0.1	Pancreas (100%)	50–80	1–20	Rash (67–90%) Glucose intolerance (38–87%) Weight loss (66–96%)
Somatostatinoma	Somatostatin	Rare	Pancreas (55%) Duodenum/jejunum (44%)	>70	45	Diabetes mellitus (63–90%) Cholelithiasis (65–90%) Diarrhea (35–90%)
GRFoma	Growth hormone–releasing hormone	Unknown	Pancreas (30%) Lung (54%) Jejunum (7%) Other (13%)	>60	16	Acromegaly (100%)
ACTHoma	ACTH	Rare	Pancreas (4–16% all ectopic Cushing's)	>95	Rare	Cushing's syndrome (100%)
pNET causing carcinoid syndrome	Serotonin, ?tachykinins	Rare (43 cases)	Pancreas (<1% all carcinoids)	60–88	Rare	Same as carcinoid syndrome above
pNET causing hypercalcemia	PTHrP Others unknown	Rare	Pancreas (rare cause of hypercalcemia)	84	Rare	Abdominal pain due to hepatic metastases
II. Rare Specific Functional Syndromes						
pNET secreting renin	Renin	Rare	Pancreas	Unknown	No	Hypertension
pNET secreting luteinizing hormone	Luteinizing hormone	Rare	Pancreas	Unknown	No	Anovulation, virilization (female); reduced libido (male)
pNET secreting erythropoietin	Erythropoietin	Rare	Pancreas	100	No	Polycythemia
pNET secreting IGF-II	Insulin-like growth factor II	Rare	Pancreas	Unknown	No	Hypoglycemia
pNET secreting GLP-1	Glucagon-like peptide-1	Rare	Pancreas	Unknown	No	Hypoglycemia, diabetes
pNET secreting enteroglucagon	Enteroglucagon	Rare	Pancreas, small intestine	Unknown	Rare	Small intestinal hypertrophy, intestinal stasis, malabsorption
III. Possible Specific Functional pNET Syndromes						
pNET secreting calcitonin	Calcitonin	Rare	Pancreas (rare cause of hypercalcitonemia)	>80	16	Diarrhea (50%)
pNET secreting neurotensin	Neurotensin	Rare	Pancreas (100%)	Unknown	No	Motility disturbances, vascular symptoms
pNET secreting pancreatic polypeptide (PPoma)	Pancreatic polypeptide	1–2	Pancreas	>60	18–44	Watery diarrhea
pNET secreting ghrelin	Ghrelin	Rare	Pancreas	Unknown	No	Effects on appetite, body weight
IV. Nonfunctional Syndrome pNET						
PPoma/nonfunctional[a]	None	1–2	Pancreas (100%)	>60	18–44	Weight loss (30–90%) Abdominal mass (10–30%) Pain (30–95%)

Abbreviations: ACTH, adrenocorticotropic hormone; GRFoma, growth hormone–releasing factor secreting pancreatic endocrine tumor; IGF-II, insulin-like growth factor II; MEN, multiple endocrine neoplasia; pNET, pancreatic neuroendocrine tumor; PPoma, tumor secreting pancreatic polypeptide; PTHrP, parathyroid hormone–related peptide; VIPoma, tumor secreting vasoactive intestinal peptide; WDHA, *w*atery *d*iarrhea, *h*ypokalemia, and *a*chlorhydria syndrome.

[a]Pancreatic polypeptide–secreting tumors (PPomas) are listed in two places because most authorities classify these as not associated with a specific hormonal syndrome (nonfunctional); however, rare cases of watery diarrhea proposed to be due to PPomas have been reported.