

# NEUROTENSINOMAS

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## ABSTRACT

Neurotensin (NT) is a 13 amino acid polypeptide first extracted from bovine brain subsequently isolated from the human GI tract. Neurotensin has a number of interesting pharmacologic effects that include hypotension, tachycardia, and cyanosis and stimulation of secretion from the small intestine. It also has been reported to inhibit the interdigestive myoelectric complex and stimulate insulin release. NT also increases venous vascular permeability, raises blood glucose, and lowers blood pressure. High concentrations of NT-like immunoreactivity (NTLI) are localized to a specific “N” cell in the jejunum. Plasma concentrations rise after food ingestion, and high circulating levels have been found after surgery for duodenal ulcer and jejunoileal bypass for obesity. No clear physiologic role has been established for the peptide. High circulating levels also have been found in patients with VIPomas. The clinical features of reported cases include diarrhea, hypotension, hypokalemia, edema, weight loss, and, occasionally, diabetes. It can mimic the Vipoma syndrome comprising WDHA ( watery diarrhea, hypotension, hypokalemia and acidosis). Surgical removal cures about 50% of cases and tumors are sensitive to streptozotocin.

Neurotensin (NT) is a 13 amino acid polypeptide first extracted from bovine brain by Carraway and Leeman (1). It subsequently was isolated from the human GI tract and found to have the same amino acid sequence as that in brain (2). Neurotensin has a number of interesting pharmacologic effects that include hypotension, tachycardia, and cyanosis (3) (4) and stimulation of secretion from the small intestine (5). It also has been reported to inhibit the interdigestive myoelectric complex and stimulate insulin release (6). NT also increases venous vascular permeability, raises blood glucose, (7) (8) (9) and lowers blood pressure (1) (4).

High concentrations of NT-like immunoreactivity (NTLI) are present in the ileal mucosa, where it is localized to a specific “N” cell (10). Plasma concentrations rise after food ingestion (11), and high circulating levels (12) have been found after surgery for duodenal ulcer and jejunoileal bypass for obesity (13). No clear physiologic role has been established for the peptide. High circulating levels also have been found in patients with VIPomas (14-18). (Assay available at Inter Science Institute-800-255-2873).

In 1981, based on the pharmacologic actions of NT, it was predicted (19) that a syndrome of excess would emerge, presenting with features that are consonant with the pharmacologic actions of the peptide: diabetes, hypotension, vasodilatation, cyanosis, and edema. In addition

to these features, investigation would reveal net secretion of fluid and electrolytes, inhibition of gastric acid secretion, infrequent interdigestive myoelectric complexes, and prolonged biologic reaction of gastric emptying. The prediction that diabetes would occur was based on the predominant stimulation of adrenomedullary secretions despite stimulation of insulin secretion (20). The clinical features of reported cases include diarrhea, hypotension, hypokalemia, edema, weight loss, and, occasionally, diabetes (21) (19).

Apart from these reported cases, Blackburn and colleagues (22) examined plasma NT levels in 326 fasting patients with tumors in a variety of sites. Of these patients, 180 had tumors of the pancreas, including glucagonomas (23), gastrinomas (24), insulinomas (25), nonsecretory tumors (26), and VIPomas (27). Plasma NTLI levels were raised in only six patients with VIPomas and none with the other tumors. Twenty-one of the tumors containing VIP were removed surgically, and six were found to contain NTLI. The clinical features of these six patients did not appear to differ from those of the remaining 15 patients.

With so few cases, it is difficult to generalize on the clinical picture. Fifty percent of the cases were cured by resection of tumors in the pancreas (28) or lung, (29) and the remainder have responded well to streptozotocin. The syndrome appears to comprise diarrhea, diabetes, and weight loss; as such, it may not be readily distinguishable from the VIPoma syndrome.

Neurotensinomas probably are best characterized as yet another tumor that is capable of causing the WDHHA (watery diarrhea, hypokalemia, hypochlorhydria, and acidosis) syndrome. Edema, hypotension, and flushing should increase the suspicion of a neurotensinoma. Of interest the rise in the use of bariatric surgery in the treatment of obesity has generated clinical syndromes which mimic the above and it would be of interest to determine if neurotensin might be implicated.

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