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# Familial Medullary Carcinoma of the Thyroid: Clinical Studies in Northern New England

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We have identified five kindreds with familial medullary carcinoma of the thyroid (MTC) or multiple endocrine neoplasia syndromes type 2 (MEN-2) in New Hampshire and Vermont during the past five years. These families have been followed by periodic calcitonin testing after stimulation by calcium and pentagastrin (1). Affected individuals have been treated by total thyroidectomy.

## Brattleboro Kindred

Eight individuals with MTC and three with C-cell hyperplasia alone have undergone total thyroidectomy within the past five years at ages ranging from 19 to 72 years (Figure). Remarkably, no individual has as yet suffered any apparent ill effect from the tumor even though regional lymph node metastases were present in two patients.

The possibility of delayed or incomplete penetrance of the MTC gene is suggested by the finding of positive stimulated calcitonin tests in two young men (IV-45 and IV-91); their mothers, the apparent obligate carriers of the MTC gene, have each had at least two normal stimulated calcitonin tests at ages 41 and 39, respectively. These findings are unexpected since the MTC gene is believed to be fully penetrant at age 40 (2). Studies of katacalcin (3) and calcitonin gene-related peptide (4) secretion are currently underway to obtain further information about C-cell mass in these patients.

To date, no evidence of pheochromocytoma has been found in this family. One 32-year-old man, who has not had a stimulated calcitonin test, had a parathyroid adenoma removed at age 18, but no other cases of hypercalcemia have been seen.

## New London Kindred

Four individuals with MTC, aged 38 to 70, have had thyroidectomies in the past two years. A fifth individual, now deceased, had metastatic MTC found by lymph node biopsy at age 67. An additional six individuals have had positive stimulated calcitonin tests.

No pheochromocytomas or parathyroid disease have been recognized in this family to date. However, one individual with a positive stimulated calcitonin test has a marginal increase in urinary catecholamine metabolites and was hypercalcemic on one occasion.

A 50-year-old member of the kindred was treated successfully with radioiodine for Graves' disease 15 years ago and is scheduled for total thyroidectomy because of elevated calcitonin levels. Radioiodine treatment has been used to remove thyroid remnants in patients who have had total thyroidectomies for MTC (5); the reasoning is that any remaining C-cells in the patient would be destroyed by radiation from adjacent follicular cells. In this patient, radioiodine treatment was not effective in destroying all C-cells.

## Other Kindreds

Three additional families are under study: one man with MTC whose mother had pheochromocytoma, and two because the propositi have had C-cell hyperplasia on review of their thyroid gland histology.

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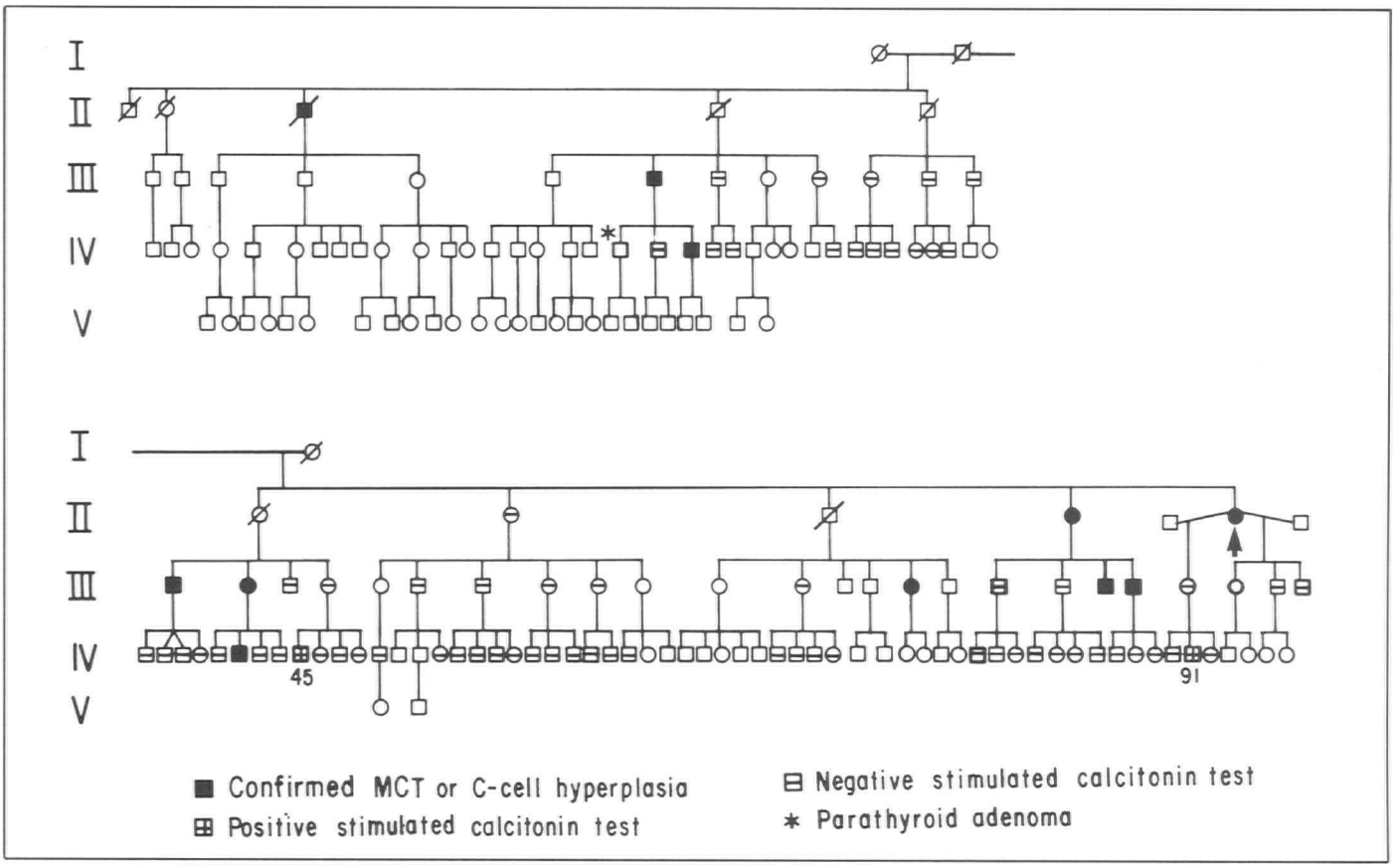


**Figure**

**Brattleboro Kindred**

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