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Screening for Medullary Thyroid Cancer in France: A National Effort

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Screening for Medullary Thyroid Cancer in France: A National Effort

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Screening for medullary thyroid cancer (MTC) in France is based on a protocol that has been widely distributed nationally. A network of coordinators utilizing a common questionnaire provides for an effective national screening program. Calcitonin stimulation procedures are systematically used for all first-degree relatives of MTC patients. Pathological studies utilize special immunopathologic techniques. Genealogic information is obtained on all index cases, and blood specimens are collected for establishing permanent cell lines. The data collected are used not only to establish the diagnosis of the hereditary or sporadic form of the disease but also to expand the screening as appropriate. This common protocol has benefited patients and their families by improving early detection of cases, increasing the number of families available for follow-up, and improving the prognosis of this cancer. Studies on these families have contributed significantly to the localization of the multiple endocrine neoplasia type 2 gene. (Henry Ford Hosp Med J 1989;37:120-1)

Since the creation of the Groupe d'Etude des Tumeurs a Calcitonine (GETC) in 1983, efforts of this French Medullary Study group have been directed toward improving methods of screening families to detect new medullary thyroid cancer (MTC) cases and gene carriers. The tools for screening, which have been described previously (1-3), include a nationwide network of coordinators utilizing standard questionnaires, a central registry, stimulated calcitonin (CT) testing, and standard pathological studies using immunopathologic techniques.

Results of Screening for MTC in France

Cases collected in the last 20 years have increased to a total of 1,377, including 349 hereditary cases found in 93 families (Table). The procedures organized by the GETC have provided data that have allowed more precise diagnoses at earlier stages by utilizing monoclonal CT assays, which have even permitted diagnosis of MTC by using stored frozen plasma from family members who had not been thought to be affected. Our experience has been similar to that of Ponder et al (4) in that the lack of a positive family history is inadequate to diagnose sporadic MTC without family screening. However, family screening is at times inconclusive because of the small number of relatives available for testing or the lack of pathology data, or because CT testing provides only borderline results occasionally even when using a monoclonal antibody in the assay. These national collaborative studies have contributed significantly to the early detection of and better prognosis for MTC patients (5).

Genealogical studies have allowed us to connect certain families and their branches from different geographical areas through common ancestors (Figure). These studies have been helpful in differentiating hereditary from sporadic cases (6).

Immunochemical CT studies of tissue sections have established the diagnosis of MTC in some atypical forms (7,8), and the bilateral MTC and C-cell hyperplasia have suggested the he-

Table
Medullary Thyroid Cancer in France, 1969-1988: 1,377 Cases*

Apparently sporadic: 1,028 cases	
MTC only: 979 cases	
MEN 2A: 20 cases	
—3 MTC and HPT	
—17 MTC and Pheo (1st sign: 8 MTC and 9 Pheo)	
MEN 2B: 29 cases	
—5 Hirschsprung Pseudosyndrome	
—24 Gorlin syndrome	
Hereditary: 349 cases (93 families)	
MTC only: 43 cases	
MEN 2A: 45 cases	
MEN 2B: 5 cases	

*Estimation as of October 1989.
MTC = medullary thyroid cancer, HPT = hyperparathyroidism, Pheo = pheochromocytoma.

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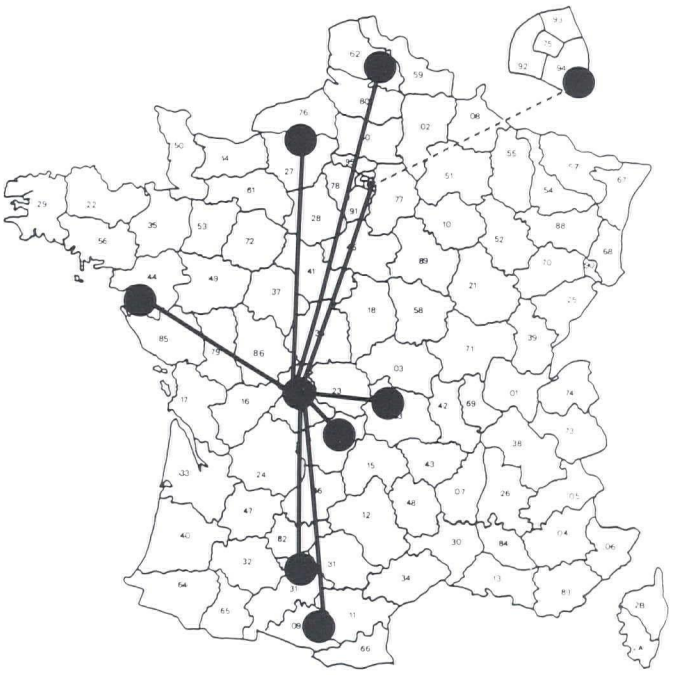
reditary nature of the disease in certain cases (9). Thyroglobulin positivity in single cells or in glandular- or follicular-like patterns has been frequently encountered in hereditary cases (8), but this finding does not seem to be a differentiating feature between hereditary and sporadic MTC. A prospective study of 34 MTC cases with somatostatin immunostaining also did not discriminate between hereditary and sporadic cases nor provide prognostic data.

The availability of the large families detected by the GETC collaborative studies (5) has provided much clinical material for genetic linkage studies and has helped confirm the location of the gene for the multiple endocrine neoplasia type 2 (MEN 2) syndrome to the pericentromeric area of chromosome 10 (10). These molecular biology techniques have been applied to the detection of MEN 2 gene carriers (11) and will eventually help lead to discovering the nature of the gene or genes involved in causing MTC and the other tumors of the MEN 2 syndrome.



Figure—Map with the number of French departments showing the distribution of affected branches of family 5 from its origin in central France.

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