**SUMMARY**

**Propose:** Today, calcitonin assay is used for the diagnosis of the medullary cancer of the thyroid (MCT) in the context of nodular thyroid disease. Calcitonin is an excellent marker of MCT but hypercalcitoninemia can also be related to other diseases, such as renal failure, endocrine tumors other MCT and sometimes ‘C’ cell hyperplasia, which is a not well-defined situation. Recent studies have contributed to define calcitoninemia thresholds, with the aims to guide decisions and avoid excessive invasive treatment.

**Current knowledge and key points:** After a brief reminder of the physiological role and the assays of calcitonin, the difficulties encountered in interpreting the hypercalcitoninemia and its potential causes other than MCT are addressed. Recent studies, on large series, now allow a better knowledge of specificity and sensitivity of calcitonin measurement in patients with nodular thyroid disease and a well-argued management.

**Future prospects and projects:** In the future, calcitonin dosage will be ordered even more frequently, as some authors recommend it as part of the routine work-up for the diagnosis of a thyroid nodule. It is up to the medical community to delineate how to use this remarkable marker, after considering all possible situations of benign hypercalcitoninemia and reserving aggressive treatments for the patients who really need them.

**COMMENT**
Calcitonin (CT) is a hormone produced by thyroid parafollicular ‘C’ cells. This peptidic molecule (containing 32 amino acids) has a physiological role in phosphocalcic and bone metabolism. Specific assays for CT (using IRMA, IMA, etc.) allow for the detection of intact monomeric CT with a great accuracy. Based on the studies carried out by the GTE in the last decade (le Groupe Français des Tumeurs Endocrines), a serum CT level of ≤ 10 pg/ml or ≤ 30 pg/ml (after a pentagastrin stimulation test) is considered normal. Above 50 pg/ml (after pentagastrin stimulation), the dosage of CT is clearly considered abnormal. Between 30 and 50 pg/ml (after pentagastrin stimulation), there is a grey zone between a ‘normal’ response and a pathological condition.

In the present review, the authors discuss a number of causes of hypercalcitoninemia outside medullary cancer of the thyroid (MCT). Elevated CT values have been reported in endocrine tumors other than MTC (mainly intestinal tumors). Hypercalcitoninemia also occurs functionally in hypercalcemic patients, conditions with chronic hypergastrinemia (Biermer’s anemia, Zollinger-Ellison syndrome, or after treatment with IPPs), chronic renal failure, and pseudo-hypoparathyroidism (type Ia). The calcitonin ‘precursor’ (CTP) is a ubiquitous molecule containing 116
amino-acids, that is not normally found in the serum. However, elevated CTP levels have been found in patients with severe sepsis (bacterial and parasitic infections) and recent data seem to indicate that CTP might possibly interfere with CT measurements. The authors therefore recommend avoiding CT measurements in patients during an infection. Concerning C cell hyperplasia, the authors review the model of familial MCT and discuss the association of abnormally elevated CT levels found in Hashimoto’s thyroiditis and non-medullary thyroid neoplasia. Finally, the authors discuss the controversy as to whether CT measurements ought to be (or not?) a part of the routine work-up of a thyroid nodule. This is an interesting topic for which presently a difference of opinions remains between the recently published American and European consensus for the diagnosis and management of thyroid nodules and cancer. (Daniel Glinoer, M.D.; Ph.D.)

See Figure below

![Image of thyroid nodules and hyperplasia]