hospitalization period, then once a week in outpatient clinics. Results were expressed as grams of albumin per mole of creatinine (UAlb/Ucr ratio).

Among the 16 subjects, eight showed evidence of rejection on the basis of a positive renal biopsy, six of whom developed concomitant infections episodes. In the eight other transplant recipients, with no evidence of rejection episodes, three demonstrated infections episodes.

Results are summarized in Table 1. We observed a weak correlation (P < 0.05) between an increased ratio and rejection episodes, with no sensitivity (56%), poor specificity (64%), and very poor positive predictive value (PPV = 33%), and excellent negative predictive value (NPV = 95%).

By contrast, there was very strong correlation between a positive ratio and rejection episodes (P < 0.001). The sensitivity and specificity were good (100% and 87%, respectively), with a PPV and an NPV of 86% and 100%, respectively.

We also observed a highly significant correlation between a positive ratio and an increase in serum creatinine (SCr) (P < 0.001), with good sensitivity and specificity.

We conclude that increased UAlb/Ucr ratios and increased SCr concentrations are strongly correlated. The sensitivity and the specificity of increases in both markers of renal allograft rejection are similar, with those for SCr concentrations being slightly better. However, if increased UAlb/Ucr is used alone as a sensitive marker of rejection crises, its specificity is very poor. Many false positive were observed during bacterial or viral infections or urological complications.

### References


### Unexpected High Calcitonin Concentrations after Pentagastrin Stimulation

B. Kemper and M. M. Ritter


Calcitonin (hCT) is the analyte commonly measured in the management and follow-up of patients with sporadic or familial medullary thyroid carcinoma, and the pentagastrin stimulation test (PGS) is the most reliable method for the early discovery of the multiple endocrine neoplasia syndrome type II/III (MEN II/III). For many years radioimmunoassays (RIAs) with polyclonal antibodies were the main method for determining calcitonin, and many authors reported results for patients and reference groups. Now immunoradiometric assays (IRMA) with monoclonal antibodies are in use because they are considered more precise and sensitive, so that reference intervals have to be evaluated anew.

Several studies concerning PGS (1-3) all agree on an upper normal value of hCT of about 100 ng/L, but these were performed with various test procedures and hCT was determined by different assays. In our clinic we perform the PGS according to Wells et al. (4), who found that all MEN II patients in their group responded to the combined administration of pentagastrin and calcium, whereas with each agent alone they found at least one patient per group with a false-negative result. Our procedure is as follows: calcium, 2 mg (50 µmol) per kilogram of body weight, is administered intravenously over 60 s, followed by a pentagastrin injection of 0.5 µg (0.65 nmol) per kilogram over 5 s. Blood samples are taken shortly before and 1, 2, 3, 5, and 10 min after injection. We analyzed the sera for hCT with the IRMA from Medgenix (Fleurus, Belgium).

We re-examined sera collected during the PGS from patients with diagnosed MEN II (n = 5) and found peak concentrations exceeded 400 ng/L, whereas in their nonaffected relatives (n = 24), peak values were <50 ng/L for women and <103 ng/L for men. To determine reference values for healthy controls, we performed the PGS on 20 people (10 women and 10 men) of our staff, aged 23-50 years. Only five responded with no detectable increase of hCT; another 11 had increases within the expected range and, to our surprise, four had very strong responses, up to 303 µg/L (three men, ages 30, 34, and 49 years, and one 47-year-old woman, whose values were 150, 303, 208, and 153 µg/L, respectively). Peak concentrations of hCT were reached mostly in the second minute (n = 14), but also in the first (n = 1) or third (n = 5) minute.

The values obtained are known to depend on the assay used, because the antibodies applied in different assays are not standardized with regard to epitopes recognized, affinity, or avidity. Therefore we re-examined the samples with another kit (Nichols calcitonin) and found even slightly higher values, two of them exceeding by far the reference values given by the manufacturer.

Others (5) have reported that in rare cases some hCT-like substances can lead to falsely high hCT values and advise using an extraction technique for isolating biologically active hCT on silica columns. To be sure of the identity of the hCT we measured, we performed the extraction as described (5) and found the same amount of hCT as without extraction.

In conclusion, some healthy volunteers undergoing PGS responded with an increase in hCT formerly considered...
suggestive of C-cell hyperplasia. Because in our institution the lowest increase thus far during a PGS in members of a MEN II family was 400 ng/L (C-cell hyperplasia confirmed after surgery), there still exists a borderline value that separates normal subjects from patients. The reason for the unexpected increase in our control group (inhabitants of an iodine-deficient area) is now under investigation, but we wish to report this phenomenon so that it can be taken into account in the diagnosis of MEN II and when surgical intervention is considered.

References

Four Methods Compared for Determining Plasma Creatinine with the Monarch Centrifugal Analyzer
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I compared the creatinine method of the Technicon (Tarrytown, NY) SMAC 2, based on alkaline picrate with dialysis, with four creatinine methods of the Monarch [Instrumentation Laboratory (IL), Lexington, MA] centrifugal analyzer. Of the two kinetic alkaline picrate assays, one involved IL reagent and reaction conditions, and the other was optimized to minimize bilirubin interference by decreasing the reading interval and increasing the picrate concentration to 35 mmol/L (I). Enzymatic creatinine assays from BCL and Wako were modified for the Monarch. Both assays make use of creatinase, creatininas, sarcosine oxidase, and peroxidase, but they differ with respect to reading wavelength, incorporation and nature of phenol derivative, and the addition of ascorbic acid oxidase and potassium ferrocyanide to the Wako reaction. Both kits were reconstituted with 80% of the volume specified by the manufacturers, to accommodate sample and reagent dilutions on the Monarch. The "load, spin, reload, (cr1) incubate, analyze" facility was used on the Monarch, as in other studies (2), to have the sample pre-incubation with creatinase precede the other reactions and to ensure that all samples are in contact with each reagent for identical times.

Between-batch imprecision of the kinetic picrate methods at 100 and 400 μmol/L (CV 2.29–4.56%) was better than in the enzymatic assays (CV 4.53–8.32%). Analytical recovery studies and comparisons with patient's samples showed that calibration with plasma is inappropriate for enzymatic creatinine assays, resulting in 10% to 20% over-recovery. Use of aqueous calibrants yielded analytical recoveries of creatinine between 97.8% and 99.6%.

Glycine; taurine; sodium salts of cholic, deoxycholic, and chenodeoxycholic acids; and bilirubin did not interfere in any assay. Acetoacetate, 1 to 20 mmol/L, gave an increasing positive interference in the SMAC (3) and the modified kinetic picrate method (4) but had a negligible effect in the IL picrate method and none in either enzymatic assay. All assays were studied in the presence of bilirubin, 50 to 500 μmol/L (Figure 1), which gave a marked negative interference in the BCL method, as in other peroxide-detection systems (5). The inclusion of potassium ferrocyanide and the longer reading wavelength for the Wako method probably account for the reduced interference by bilirubin in that method.

References

Chemiluminescence and Radioimmunology Compared for 10 Allergens, D. Roche,1 H. Susini de Luca,2 and N. Tugendhaft2 (1 Hôpital Lariboisière, Service de med. nucléaire, 2 rue Amboise Paré, 75475 Paris Cédex 10; 2 Institute Pasteur, Service d'allergologie, 28 rue du Dr. Roux, 75724 Paris Cédex 15; 3 22 rue des Martyrs, 75009 Paris, France)

Patients with Type 1 allergy typically have increased titers of total IgE and allergen-specific IgE, both cell-bound and circulating in the blood (1), consistent with the cause of their particular allergy. The clinical diagnosis of allergy is supported by demonstrating the presence of allergen-specific IgE antibodies in patients' sera (2, 3).

Recently a chemiluminescent immunoassay kit for measuring specific IgE has been introduced commercially (Ciba Corning Magic Lite System). This immunoassay involves