centration increased in proportion to the PV-10 concentration on the DxC 800 and in proportion to HI values on the Roche Modular D. From the saline dilutions, we calculated the PV-10 concentration in the affected patient blood to be approximately equal to a dilution of 1 part in 5000, or approximately 20 μmol/L.

To determine the mechanism of the interference, we manually added the bilirubin reagents and the pooled plasma spiked with PV-10 in the same ratios as per the manufacturers’ methods. Absorbances were measured on the Beckman Coulter DU 640 spectrophotometer. The 2 bilirubin methods measure primary/secondary absorbances at 520 nm/580 nm with the Beckman Coulter method and 546 nm/600 nm with the Roche method. Blanking is performed after the addition of reagent A and reagent B and without sample in the Beckman Coulter method, and after reagent 1 and sample are added in the Roche method. Both assays use diazo methods, with azobilirubin being the final product. In both methods, the PV-10 is either chemically altered or compounds are formed with the first reagent in both methods; the compound(s) has a peak absorbance at 562 nm. Blanking with the Beckman Coulter method would not correct for nonspecific chromogens from samples with PV-10, hence the interference. In contrast, blanking with the Roche method is able to correct for nonspecific chromogens(s) from the sample; in fact, the negative values in Table 1 suggest that it may overcorrect. With the Beckman Coulter serum indices method, the sample is added to Sample Diluent 1; wavelength readings are taken at 340, 410, 470, 600, and 670 nm; and the absorbances are used to compute each index. The PV-10 peaks are not detected, and there is no interference. With the Roche serum indices method, the sample is added to saline, and absorbances are measured at 570 nm and 600 nm for the HI. The presence of PV-10 causes a substantial absorbance increase at 570 nm.

On the Beckman Coulter analyzers, the icteric index and the direct bilirubin concentration (in which sample blanking is performed with reagent A) remain unchanged in the presence of PV-10. Discordant Beckman Coulter total bilirubin results with no change in the icteric index or the direct bilirubin value and/or an increased HI from the Roche analyzer in the absence of changes in other analytes (e.g., K⁺, lactate dehydrogenase, and so on) may indicate the presence of PV-10. The manufacturer of PV-10 has been informed of these findings. The PV-10 interference illustrates how different method-blanking procedures can help eliminate interferences.

Some details of the success of the PV-10 trial have been published (1), and full details undoubtedly will be published in the near future. In light of the present findings, the trial protocol for the timing of postinjection sample collection should be reviewed. Plans are under way for additional trials of PV-10 for treating other cancers. Therefore, these interferences may become more common with the assays outlined above and potentially with others on different analytical systems.

Author Contributions: All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

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Some Notes on Visinin-Like Protein 1 and Alzheimer Disease

To the Editor:

We wish to comment and add some potentially useful information on certain aspects of the report of Lee and collaborators, which was recently published in Clinical Chemistry (1). In an earlier study, the authors had proposed visinin-like protein 1 [VILIP-14 or VSNL1; VSNL1 gene (visinin-like 1)] as a

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To the Editor:

We wish to comment and add some potentially useful information on certain aspects of the report of Lee and collaborators, which was recently published in Clinical Chemistry (1). In an earlier study, the authors had proposed visinin-like protein 1 [VILIP-14 or VSNL1; VSNL1 gene (visinin-like 1)] as a
potential biomarker for stroke because they had detected this intracellular calcium-binding protein in cerebrospinal fluid (CSF) in a rat model of stroke and in the plasma of patients after stroke (2). The group extended these findings to Alzheimer disease (AD) in a second publication (1). VILIP-1 concentrations were significantly altered in the CSF of AD patients; hence, the authors concluded that VILIP-1 might also be a useful novel biomarker for AD-related brain injury. Lee et al. put forward the hypothesis that measures of VILIP-1 might reflect neuronal injury with subsequent release of the intracellular protein VILIP-1 into the CSF. The authors stated that both Aβ and τ reflect different pathologic features of AD, whereas VILIP-1 may reflect the end result of the disease, namely neuronal cell death. We would like to add important information concerning the hypothesized relationship between the calcium sensor protein VILIP-1 and AD (3–5). Owing to the limited space, we cannot discuss here the findings on the production of VILIP-1 in rat brain (1); instead, we would like to emphasize that VILIP-1 immunoreactivity is also abundantly present in the nondemented human brain with a regional and cellular distribution of the protein similar to that in rat brain (3). With a knowledge of the topography of VILIP-1 in human brain, we have addressed 3 questions about VILIP-1 in the brains of AD patients: (a) Is the cellular localization of the protein altered in AD? (b) Is the protein content altered in AD brains? and (c) is there any anatomical association of the neuropathologic hallmarks of the disease (plaques, tangles) with VILIP-1? We found that the number of VILIP-1–immunoreactive neurons was significantly reduced in the temporal cortex of AD patients, whereas the total number of neurons was unchanged (4). These data point to a disease-related loss of VILIP-1–producing neurons. Moreover, western blot analyses of brain tissue extracts of AD patients revealed that VILIP-1 is less concentrated in AD brains (5). Importantly, other groups have confirmed the reported changes in VILIP-1 protein production in AD brains by means of gene microarray analysis (6). Both the reduced number of VILIP-1–immunoreactive cortical neurons and the decreased tissue content in AD fit with the CSF data presented by Lee and colleagues. Furthermore, extracellularly located VILIP-1 was detected in close association with typical pathologic hallmarks of AD, such as dystrophic nerve cell processes, amorphous and neuritic plaques, and extracellular tangles, pointing to an involvement of this calcium sensor protein in the pathophysiology of changed calcium homeostasis in AD (4, 5). Moreover, these data provide reason to suppose that VILIP-1 may not only be a CSF marker of cell injury in AD (1) but may also be causally related to AD. Because VILIP-1 is associated with fibrillar tangles in AD brains, we tested whether VILIP-1 has an influence on τ hyperphosphorylation. VILIP-1 production enhanced hyperphosphorylation of τ protein and enhanced calcium-mediated cell death in transfected neuronal cell lines. These findings suggest that this calcium sensor protein may indeed influence τ phosphorylation and have a role in calcium-mediated neurotoxicity in AD. The observed reduction in VILIP-1–producing cells in AD thus may indicate selective vulnerability (5). The close association of VILIP-1 with τ pathology is of special interest because it is in good agreement with the findings of Lee et al. (1) that VILIP-1 values correlate highly with phosphorylated τ in patients, but not with Aβ values.

We hope that our added information on VILIP-1 will enable the readers of Clinical Chemistry to put these highly interesting data on the potential biomarker VILIP-1 in perspective with respect to a possible pathophysiological relationship between VILIP-1 and AD.

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Comparison of a New Procalcitonin Assay from Roche with the Established Method on the Brahms Kryptor

To the Editor:

Procalcitonin (PCT) is a 13-kDa peptide and a precursor of calcitonin. In a healthy population, PCT concentrations are negligible (1). In systemic bacterial and fungal infections, plasma concentrations are raised, whereas concentrations remain fairly low in infections of viral or nonspecific cause (2). Recent studies have demonstrated the potential of PCT as a parameter to guide antibiotic therapy in different groups of patients, i.e., patients with chronic obstructive pulmonary disease experiencing respiratory tract infections (3, 4). The most frequently used medical decision points at which the use of antibiotic therapy is considered are 0.25 µg/L and 0.50 µg/L, depending on the patient population (3, 4).

The first PCT assays were based on manual immunochemistry methods (Brahms PCT LIA). These assays have been replaced by fully automated immunochemistry methods (Brahms Kryptor, Brahms LIAISON, Olympus SphereLight 180). Recently, the PCT assay has been modified for use on a consolidated routine immunochemistry analyzer family, the Roche Elecsys, cobas, and the Roche Modular E170 systems. We evaluated the analytical performance of this new assay by following the EP10 protocol, a document from the Clinical and Laboratory Standards Institute to test precision, linearity, recovery, carryover, and drift. Samples were prepared at different concentrations, from 0.24–2.85 µg/L. Three aliquots of each concentration were assayed on 5 different days, in a specific assay order. The within-run CV ranged from 3.0% for the lowest concentration to 1.3% for the highest concentration. The between-day CV ranged from 6.3% for the lowest concentration to 2.8% for the highest. These levels of imprecision were comparable with those reported for the PCT assay on the Brahms Kryptor (5). The mean recovery was 99%. There was no evidence of nonlinearity or sample carryover. The limit of quantification, i.e., the lowest concentration of analyte that can be quantified with a between-run imprecision of <20%, met the manufacturer’s specification of 0.06 µg/L. In addition, we compared the new PCT assay from Roche on the Modular 170 with the widely accepted PCT assay from Brahms on the Kryptor (5). For analytical comparison, we used 229 samples of patient serum obtained from 195 different patients who were admitted to our hospital for lower respiratory tract infections (81, exacerbation of chronic obstructive pulmonary disease; 114, pneumonia). The patients participated in an ongoing study in our hospital on the etiology of exacerbations of chronic obstructive pulmonary disease, a study approved by the local ethics committee. Samples were also collected from 34 patients after antibiotic treatment. The majority of the serum samples were obtained within 24 h of admission. Samples not immediately analyzed were stored at −80 °C until analysis. PCT concentrations ranged from 0.02 µg/L (limit of detection, i.e., the lowest concentration of analyte that can be reliably measured as being qualitatively present in the sample) to 57 µg/L. PCT concentrations were <0.10 µg/L in 126 samples, ≥0.10 µg/L and <0.25 µg/L in 34 samples, ≥0.25 µg/L and <0.50 µg/L in 19 samples, and ≥0.5 µg/L in 50 samples. Nearly all of these patients, including the 126 patients with PCT concentrations <0.10 µg/L, were treated with antibiotics, reflecting the potential benefit of PCT-guided antibiotic therapy for preventing antibiotic overuse. Confirmation of this possible benefit awaits further study. Methods were compared by orthogonal Deming analysis (y = 0.95x − 0.09 µg/L, where x is the PCT assay from Brahms on the Kryptor and y is the PCT assay from Roche on the Modular instrument; Se 0.95 = 1.02; r = 0.99) and by medical decision points. No outliers were detected (i.e., distance from the regression line exceeding 10 times the Se 0.95 value). The concordance between the 2 assays was 99% and 98% at the cutoff values of 0.25 µg/L and 0.50 µg/L, respectively. Fig. 1 shows the comparative data for the clinically important interval of 0–1.0 µg/L. The predicted medical decision points and 95% CIs for the Roche assay were 0.24 (0.23–0.25) µg/L and 0.49 (0.48–0.51) µg/L, respectively, as calculated by Deming regression analysis.

In conclusion, the new PCT assay on the Roche Modular shows a