We received a 2nd blood sample when the infant was 18 months old, and again this sample showed evidence of significant hemolysis, with decreased hemoglobin (60 g/L), hematocrit (0.18), and erythrocyte count ($2.4 \times 10^{12}$). The normochromic blood film showed pencil cells, some elliptocytes, and erythrocyte fragments. Mass spectrometry confirmed a complete switch to an adult pattern of hemoglobin synthesis, with no significant amount of $\gamma$ chains detected; the abnormal 15 157-Da $\alpha$ chain was still present at a level of approximately 18% (Fig. 1). Isopropanol stability tests showed no precipitation at 30 min, and although a small amount of precipitate formed after the incubation was extended to 45 min, electrospray analysis showed no enrichment of the variant chain. This normal stability suggests that the mutation is benign; making it unlikely that it contributes to the hemolytic condition.

This case highlights the importance of isolating the potential pathological effect of novel hemoglobin mutations when they are identified in association with changes in hemoglobin concentrations. In this case it appears the hemolysis is due to the accompanying, but unrelated, erythrocyte membrane defect.

Grant support/funding: None declared. Financial disclosures: None declared. Acknowledgments: We gratefully acknowledge the assistance of Jaine Duncan and Vanessa Buchan.

References


Stephen O. Brennan1,2*
Tim Chan1
Michael Beard1

1 Canterbury Health Laboratories, Christchurch, New Zealand
2 Pathology Department Christchurch School of Medicine University of Otago Christchurch, New Zealand

* Address correspondence to this author at: PO Box 151, Canterbury Health Laboratories, Christchurch, New Zealand. Fax 64-3-3640545; e-mail steve.brennan@chmeds.ac.nz.

Comparison of the Diagnostic Accuracy of BNP and NT-proBNP in Acute and Chronic Heart Failure

To the Editor:

I read with great interest the paper by Clerico et al. (1), which described a comparable diagnostic accuracy of brain natriuretic peptide (BNP) and the N-terminal part of the propeptide of BNP (NT-proBNP) in patients with heart failure. The authors are to be congratulated for addressing this important issue.

There are two details that concern me that might benefit from additional explanations from the authors. First, the paper cites an important study that compared both markers in elderly patients only (2). This patient subset is of major importance because diagnostic uncertainty seems to be highest in elderly patients (3). BNP was found to have significantly higher diagnostic accuracy than NT-proBNP (area under the curve 0.85 vs 0.80) in elderly patients. Unfortunately, in Table 2 and in Fig. 3, these data seem to be incorrectly displayed, indicating the opposite result (superiority of NT-proBNP). The authors may wish to correct this presentation of their data and recalculate their metaanalysis accordingly. Second, the expression “chronic heart failure” does not seem appropriate for the second part of the analysis, because the studies summarized in Table 1 and Fig. 2 tested both peptides in the detection of left ventricular systolic and/or diastolic dysfunction. Please note that chronic
heart failure must not be used interchangeably as a term for these conditions.

Grant/funding support: None declared.

Financial disclosures: I have received research support from Biosite, Brahms, Abbott, and Roche, and speaker’s honoraria from Abbott, Bayer, Biosite, Brahms, Dade Behring, and Roche.

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Christian Mueller
Department of Internal Medicine
University Hospital Basel
Petersgraben 4, CH-4031
Basel, Switzerland
Fax 0041-61-2655353
E-mail chmueller@uhbs.ch.
DOI: 10.1373/clinchem.2007.091876

The authors of the article cited above respond:

To the Editor:

We are grateful to Dr. Christian Mueller for his constructive suggestions regarding our review (1). Actually, area under the curve (AUC) values of brain natriuretic peptide (BNP) and the N-terminal part of the propeptide of BNP (NT-proBNP) (0.85 and 0.80, respectively) assays related to the study by Ray et al. (2) were erroneously inverted, whereas sensitivity and specificity were correctly indicated in Table 2 of our review (1). Nevertheless, we confirm that the conclusions of our review were correct; they were based on the diagnostic odds ratios, which were derived from sensitivity and specificity values.

As suggested by Dr. Mueller, we recalculated the pooled AUC values by using the random-effects model according to the DerSimonian-Laird method, and we report the Forest plots for BNP and NT-proBNP assays in Fig. 1, A and B, respectively. Indeed, the calculated AUC values for NT-proBNP [0.8615 (0.8144–0.9007)] and BNP [0.8477 (0.7909–0.9045)] assays were very similar to those reported in our review (1), and statistical reappraisal confirmed that the AUCs are not significantly different between BNP and NT-proBNP assays for diagnosis of acute heart failure.

With regards to Mueller’s challenge of our definition of “chronic heart failure” regarding the studies reported in Table 1 and Fig. 2 of our review (1), we note that all of these studies aimed to detect structural myocardial impairment leading to...