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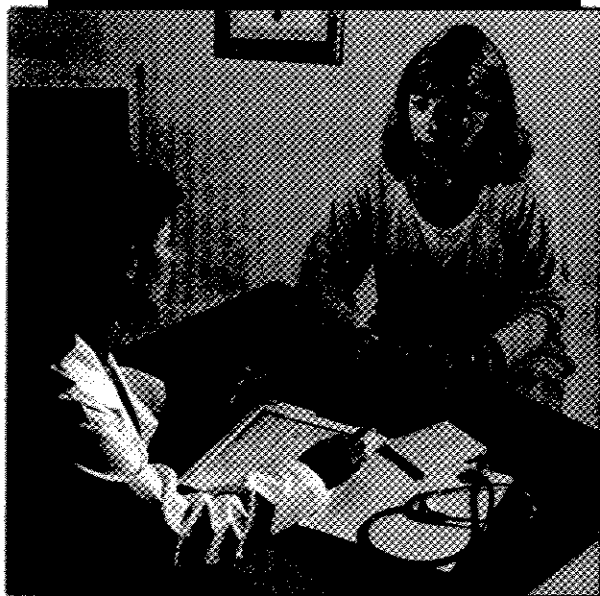
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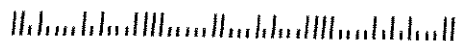
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# Examining the uses of BNP testing in the outpatient setting

The efficacy of the B-natriuretic peptide assay for congestive heart failure diagnosis in acute care settings is well-established. Can its use be extended to the outpatient setting, particularly for identifying heart failure early in high-risk patients?

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**C**ongestive heart failure (CHF) is a prevalent disease whose nonspecific signs and symptoms often present diagnostic and management difficulties.<sup>1,2</sup> The advent of a rapid point-of-care B-natriuretic peptide (BNP) assay has helped clarify diagnostic ambiguity and become part of the diagnostic armamentarium for the physician caring for acutely dyspneic patients.<sup>3-6</sup> BNP has also been shown to serve as a surrogate for wedge pressure, extracellular volume, and neurohormonal modulation.<sup>7-10</sup>

BNP is a 32-amino-acid polypeptide secreted from the cardiac ventricles in response to ventricular volume expansion and pressure overload.<sup>11</sup> Elevated BNP values indicate ventricular wall stress and volume overload, such as that which occurs with CHF and in patients with left ventricular dysfunction, and the values correlate with the severity of symptoms and prognosis.<sup>12-14</sup> BNP analysis is undergoing investigation as a diagnostic tool in the outpatient setting, and its utility and disadvantages outside the emergency department (ED) have not yet been clarified.

Possible outpatient uses that have undergone clinical investigation include CHF diagnosis and monitoring, determination of the effectiveness of CHF treatment and titration, early detection of CHF in high-risk patients, and monitoring for preeclampsia during pregnancy. The assay is currently undergoing review to become a waived test under CLIA.\*

### Potential outpatient uses

The use of BNP values to help diagnose and exclude dyspnea due to CHF is well-established in the ED and urgent care settings.<sup>3,6</sup> Rapid BNP testing may also prove beneficial in these scenarios:

\*Clinical Laboratory Improvement Amendments of 1988.

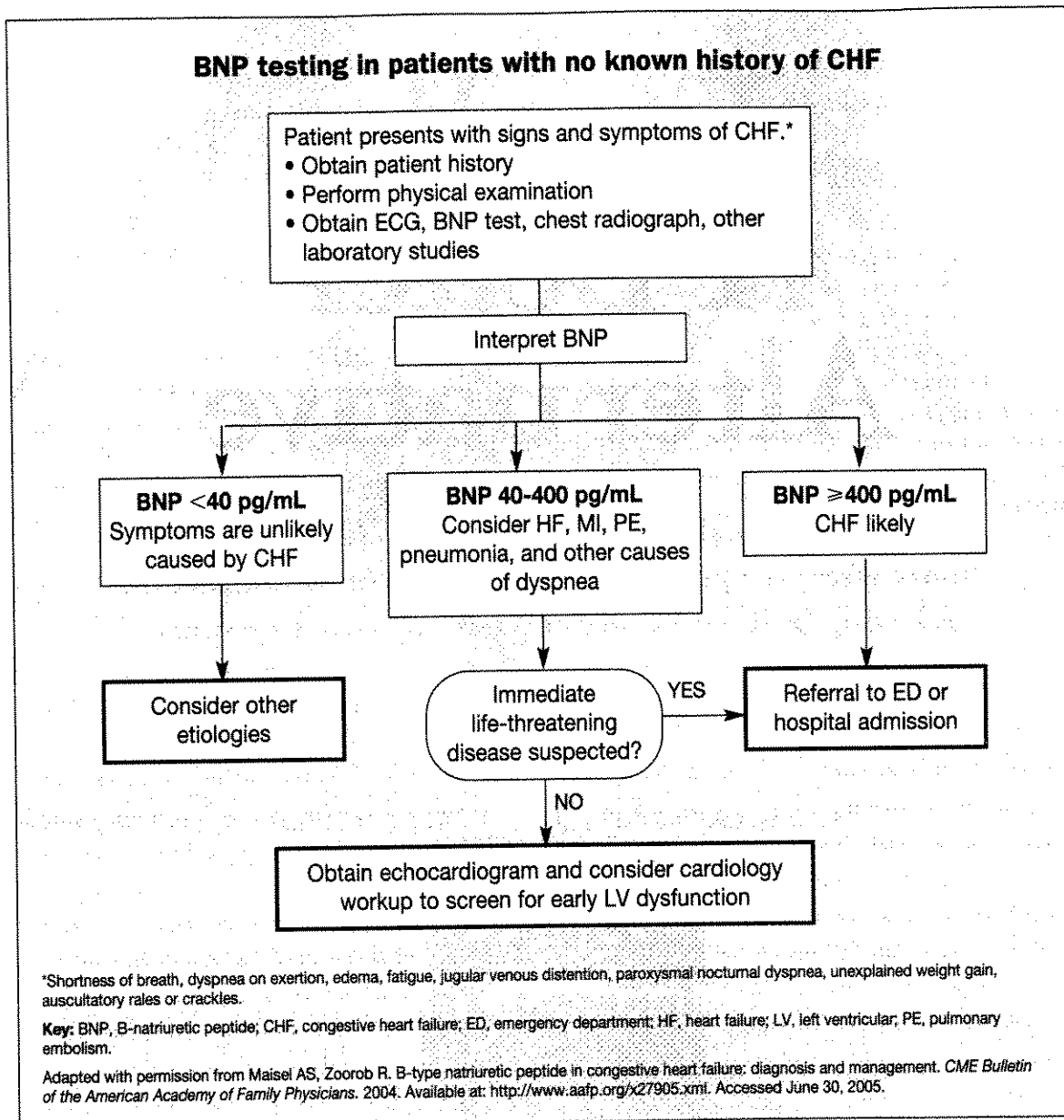
- Evaluating a dyspneic outpatient to confirm signs and symptoms of new-onset CHF.
- Evaluating for occult CHF or cor pulmonale in a patient with chronic obstructive pulmonary disease who is not responding to treatment.
- Ruling out CHF.<sup>15,16</sup> The negative predictive value of normal BNP levels has led to the development of protocols incorporating a low BNP value of less than 100 pg/mL as an indication that CHF is highly unlikely and that alternative diagnoses should be entertained.<sup>15</sup> The BNP cut-points of 40 pg/mL and 400 pg/mL have a high negative and positive predictive value for determining CHF, respectively (see the algorithm, page 40).<sup>17</sup>
- Measuring the severity of disease and prognosis. BNP values have shown to strongly correlate with the widely used New York Heart Association heart failure classification.

### Anticipate CHF readmissions

A study of 325 patients presenting to the ED with dyspnea showed that 51% of those who had BNP values above 480 pg/mL suffered a cardiac event within 6 months, compared with only 2.5% of patients who had BNP values below 230 pg/mL.<sup>18</sup>

#### Article at a glance

- The advent of the rapid point-of-care B-natriuretic peptide (BNP) assay has proven useful when assessing patients with dyspnea in the emergency department.
- BNP testing is investigational in the outpatient setting, and disadvantages to using the test have not been clarified.
- Serial BNP measurements may provide insight regarding progression of congestive heart failure and treatment.
- BNP testing may prove useful in early detection of asymptomatic left ventricular dysfunction in certain high-risk patients.



Another study demonstrated that a discharge BNP value below 400 pg/mL is associated with a decreased likelihood of readmission for CHF within 30 days.<sup>19,20</sup> These findings may be important as there is growing evidence that a discrepancy exists between the clinical severity of CHF as determined by the patient's symptoms and the physician's examination and the pathophysiologic and biochemical severity of CHF as determined by BNP values.

The recent Rapid Emergency Department Heart Failure Outpatient Trial (REDHOT) de-

monstrated a disconnect between the perceived CHF severity by physicians and that of BNP levels and alluded to the potential for BNP-guided triage and initial treatment options.<sup>16</sup> A BNP level that is still significantly elevated—above 400 pg/mL, for example—in a setting where a patient feels well and appears euvolemic clinically may indicate the need for further titration of CHF therapies.

A recent large prospective study with follow-up lasting more than 5 years demonstrated the risk of death and cardiovascular events indicated

by BNP levels was well below current thresholds used to diagnose CHF.<sup>18,21</sup> This study raises the question of meaningful "normal" BNP levels and perhaps indicates that clinicians could be informed of impending problems years before patients become symptomatic and before the disease process is severe and clinically apparent. The findings demonstrated that although patients had BNP levels within "normal" limits of below 100 pg/mL, those patients with levels above the 80th percentile were associated with multivariable adjusted hazard ratios of 1.62 for death, 1.76 for major cardiovascular event, 1.91 for atrial fibrillation, 1.99 for stroke of transient ischemic attack, and 3.07 for CHF.

#### Using BNP values to monitor disease progression

One of the most promising potential benefits of outpatient BNP testing is in the area of objectively and quantitatively monitoring the progression of CHF. Just as serum creatinine values are used to monitor renal dysfunction, BNP values have demonstrated utility when measured serially over time and when compared to baseline steady-state BNP levels. Such measurements allow a physician to detect asymptomatic subtle trends towards decompensation. Also, certain elevated BNP levels, despite optimal therapies, may help determine when referral to a CHF specialist or clinic may be indicated.

Echocardiography is the current gold standard for assessing cardiac function and determining the severity of CHF. The information provided by

echocardiography is an invaluable analysis of cardiac function and provides estimated measurements of a variety of pressures, but limited access to these examinations and their cost deter their use on a routine basis. However, numerous studies have corroborated the correlation between echocardiographic findings and BNP values and may indicate that following BNP levels can act as a cost-effective surrogate for echocardiogram.<sup>22,23</sup>

Similarly, serial BNP testing could help clinicians follow the effectiveness of treatment and help guide the titration of therapeutics.<sup>24</sup> Other studies have shown that the beneficial effects of CHF medications correlate with declining BNP values in the hospital setting, and those findings have been confirmed in the outpatient setting.<sup>7,25-28</sup> Perhaps the largest and most persuasive of these studies is the Valsartan Heart Failure Trial (Val-HeFT) that demonstrated that reduction in BNP levels occurred over time in patients randomized to treatment with valsartan while patients who were randomized to placebo had continued elevated BNP levels.<sup>27</sup> Other outpatient trials are ongoing. □

*This article was contributed by Dr Harrison and edited by Dorothy L. Pennachio.*

*Dr Harrison discloses that he is a consultant for Biosite, which manufactures a BNP test.*

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#### REFERENCES

- McCullough PA, Philbin EF, Spertus JA, et al. Confirmation of a heart failure epidemic: findings from the Resource Utilization Among Congestive Heart Failure (R.E.A.C.H.) Study. *J Am Coll Cardiol*. 2002;39:60-69.
- Stevenson LW, Perloff JK. The limited availability of physical signs for estimating hemodynamics in chronic heart failure. *JAMA*. 1989;261:884-888.
- Maisel AS, Krishnaswamy P, Nowak RM, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N Engl J Med*. 2002;347:161-167.
- McCullough PA, Nowak RM, McCord J, et al. B-type natriuretic peptide and clinical judgment in emergency diagnosis of heart failure: analysis from Breathing Not Properly (BNP) Multinational Study. *Circulation*. 2002;106:416-422.
- McCullough PA, Hollander JE, Nowak RM, et al; BNP Multinational Study Investigators. Uncovering heart failure in patients with a history of pulmonary disease: rationale for the early use of B-type natriuretic peptide in the emergency department. *Acad Emerg Med*. 2003;10:198-204.
- Morrison LK, Harrison A, Krishnaswamy P, et al. Utility of a rapid B-natriuretic peptide assay in differentiating congestive heart failure from lung disease in patients presenting with dyspnea. *J Am Coll Cardiol*. 2002;39:202-209.
- Kazanegra R, Cheng V, Garcia A, et al. A rapid assay for B-type natriuretic peptide correlates with falling wedge pressures in patients treated for decompensated heart failure: a pilot study. *J Card Fail*. 2001;7:21-29.
- Yasue H, Yoshimura M, Sumida H, et al. Localization and mechanism of secretion of B-type natriuretic peptide in comparison with those of A-type natriuretic peptide in normal subjects and patients with heart failure. *Circulation*. 1994;90:195-203.
- Maeda K, Takayoshi T, Wada A, et al. Plasma brain natriuretic peptide as a biochemical marker of high left ventricular end-diastolic pressure in patients with symptomatic left ventricular dysfunction. *Am Heart J*. 1998;135:825-832.

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## BNP testing ■

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10. Nagagawa O, Ogawa Y, Itoh H, et al. Rapid transcriptional activation and early mRNA turnover of BNP in cardiocyte hypertrophy: evidence for BNP as an "emergency" cardiac hormone against ventricular overload. *J Clin Invest*. 1995;96:1280-1287.
11. Levin ER, Gardner DG, Samson WK. Natriuretic peptides. *N Engl J Med*. 1998;339:321-328.
12. Goto T, Takase H, Toriyama T, et al. Circulating concentrations of cardiac proteins indicate the severity of congestive heart failure. *Heart*. 2003;89:1303-1307.
13. Maisel A. B-type natriuretic peptide levels: diagnostic and prognostic in congestive heart failure: what's next? *Circulation*. 2002;105:2328-2332.
14. Yoshimura M, Yasue H, Ogawa H. Pathophysiological significance and clinical application of ANP and BNP in patients with heart failure. *Can J Physiol Pharmacol*. 2001;79:730-735.
15. Mueller C, Scholer A, Laule-Kilian K, et al. Use of B-type natriuretic peptide in the evaluation and management of acute dyspnea. *N Engl J Med*. 2004;350:647-654.
16. Maisel AS, Hollander JE, Guss D, et al. Primary results of the Rapid Emergency Department Heart Failure Outpatient Trial (REDHOT). A multicenter study of B-type natriuretic peptide levels, emergency department decision making, and outcomes in patients presenting with shortness of breath. *J Am Coll Cardiol*. 2004;44:1328-1333.
17. Maisel AS, Zoorob R. B-type natriuretic peptide in congestive heart failure: diagnosis and management. *CME Bulletin of the American Academy of Family Physicians*. 2004 vol 3, No. 3.
18. Harrison A, Morrison LK, Krishnaswamy P, et al. B-type natriuretic peptide predicts future cardiac events in patients presenting to the emergency department with dyspnea. *Ann Emerg Med*. 2002;39:131-138.
19. Cheng V, Kazanagra R, Garcia A, et al. A rapid bedside test for B-type peptide predicts treatment outcomes in patients admitted for decompensated heart failure: a pilot study. *J Am Coll Cardiol*. 2001;37:386-391.
20. Caldwell MA, Howie JN, Dracup K. BNP as discharge criteria for heart failure. *J Card Fail*. 2003;9:416-422.
21. Wang T, Larson M, Levy D, et al. Plasma natriuretic peptide levels and the risk of cardiovascular events and death. *N Engl J Med*. 2004;350:655-663.
22. Dokainish H, Zoghbi WA, Lakkis NM, et al. Comparative accuracy of B-type natriuretic peptide and tissue Doppler echocardiography in the diagnosis of congestive heart failure. *Am J Cardiol*. 2004;93:1130-1135.
23. Lubien E, DeMarta A, Krishnaswamy P, et al. Utility of B-natriuretic peptide in detecting diastolic dysfunction: comparison with Doppler velocity recordings. *Circulation*. 2002;105:595-601. Erratum in: *Circulation*. 2002;106:387.
24. Troughton RW, Frampton CM, Yandle TG, et al. Treatment of heart failure guided by plasma aminoterminal brain natriuretic peptide (N-BNP) concentrations. *Lancet*. 2000;355:1126-1130.
25. Bettencourt P. NT-proBNP and BNP: biomarkers for heart failure management. *Eur J Heart Fail*. 2004;6:359-363.
26. Richards M, Troughton RW. NT-proBNP in heart failure: therapy decisions and monitoring. *Eur J Heart Fail*. 2004;6:351-354.
27. Reed SD, Friedman JY, Velazquez EJ, et al. Multinational economic evaluation of valsartan in patients with chronic heart failure: results from the Valsartan Heart Failure Trial (Val-HeFT). *Am Heart J*. 2004;148:122-128.
28. Yoshimura M, Mizuno Y, Nakayama M, et al. B-type natriuretic peptide as a marker of the effects of enalapril in patients with heart failure. *Am J Med*. 2002;112:716-720.