

Danbury Hospital
Department of Pathology & Laboratory Medicine
Technically Speaking

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Reprocessing Unsatisfactory Thinprep Pap Specimens

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In an ongoing effort to improve patient satisfaction and reduce the number of Thinprep gynecological specimens rejected for insufficient epithelium, the Cytology section of the laboratory adopted two sample reprocessing protocols, developed by Fletcher Allan Health Care in Burlington, Vermont and recommended for use by the Cytec Corporation, manufacturer of the Cytec Thinprep Processor. Receipt of an increased number of unsatisfactory gynecological specimens had been observed initially with the use of the Cytec Thinprep; increased blood and/or mucous tended to obscure the Thinprep filter. Monitor of the utilization of these recommended protocols resulted in decrease of the rate of unsatisfactory specimens to an average of 0.36% at Danbury Hospital, a 67% improvement. This improvement eliminates repeat office visits and contributes to greater customer satisfaction.

REMINDER:

CHEM 6 and **CHEM 7** have been removed from the outpatient order screens. Due to changes in Medical Necessity, these groups are no longer available. Please order each electrolyte of interest separately or order Electrolyte Panel, a Medicare-approved panel.

MEDICARE REMINDER:

Please use appropriate the Medicare ICD-9 Codes required for laboratory testing. If you have Internet access, use: www.MedicalNecessity.Com for current ICD-9 Codes.

BNP: A New Blood Test for Congestive Heart Failure

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The Clinical Chemistry section is now offering a new test that measures the concentration of B-type natriuretic peptide (BNP) in whole blood. This test will aid in the diagnosis of congestive heart failure (CHF) in patients who present with dyspnea and other symptoms suggestive of CHF. BNP levels have been shown to be elevated in patients with CHF, but not in patients with related diseases (COPD, hypertension, diabetes, renal insufficiency).

What is BNP?

BNP is a 32-amino acid cardiac neurohormone synthesized and secreted by the ventricular myocardium in response to elevations of end-diastolic pressure and volume overload. BNP was originally identified in the porcine brain in 1988, but subsequent studies have shown that the heart is the major source of circulating BNP. In addition to BNP, the natriuretic peptides also include ANP or A-type (atrial natriuretic peptide, secreted primarily by the atrial myocardium in response to dilatation, and C-type natriuretic peptide (CNP), produced and released by endothelial cells in response to shear stress. These peptides have both natriuretic and diuretic properties: they promote Na and H₂O excretion by increasing the glomerular filtration rate and they inhibit renal Na reabsorption. The natriuretic peptide system counteracts the renin-angiotensin-aldosterone system in regulating arterial blood pressure and extracellular fluid volume.

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BNP (cont'd)

BNP and Congestive Heart Failure (CHF)

CHF occurs when the heart cannot efficiently deliver a sufficient blood supply to the body, leading to fluid accumulation and causing symptoms such as dyspnea, cardiac cough, peripheral edema, and rapid weight gain due to fluid retention. CHF is most commonly the result of diminished left ventricular systolic function, but can also have other, diverse etiologies. As cardiac function declines, there is an increase in cardiac myocyte stretch or intercavitary pressure, causing hemodynamic alterations that stimulate the release of natriuretic peptides, including BNP. BNP acts to reduce the load on the heart by causing vasodilation, diuresis and natriuresis.

While the clinical diagnosis of CHF is relatively easy and obvious in advanced stages of the disease, it can be a difficult diagnosis early in the disease progression, when intervention might help prevent or slow the disease from advancing. The New York Heart Association (NYHA) functional classification system for CHF grades the disease based on severity of symptoms and is designed to help determine treatment options. The NYHA system defines four classes of CHF, ranging from Class I (patients have no limitation of physical activity, i.e., no undue fatigue, shortness of breath, heart palpitations or pain with ordinary physical activity) to Class IV (patients have severe to complete limitation of physical activity with symptoms occurring upon any physical activity and even at rest). Circulating concentrations of BNP have been shown to increase with the severity of CHF based on the NYHA classification (see table below).

(BNP in pg/mL)	All CHF	NYHA Functional Class			
		I	II	III	IV
N	804	118	197	300	187
Mean BNP	526	146	327	576	898
SD	452	163	320	441	409
Median BNP	360	95.4	222	459	1006
5 th %ile	22.3	14.8	9.9	37.6	147
95 th %ile	>1300	498	1080	>1300	>1300
Percent >100 pg/mL	80.6%	48.3%	76.6%	86.0%	96.3%

The BNP Assay

The BNP test is a rapid, fluorescence immunometric assay called the Triage[®] BNP Test (Biosite Diagnostics). It is performed on uncentrifuged whole blood using a single-use disposable cartridge that is inserted into an automatic reader. The assay measures BNP levels in the range 5-1300 pg/mL. Test results are available approximately 15 minutes after the sample is introduced. The sample requirement is 0.5 mL of EDTA whole blood collected in lavender-stoppered tube. The BNP test is available 24/7 and can be ordered in the computer system as “BNP”. Due to the instability of BNP, this test cannot be “added on” to a sample that is more than 4 hours old.

Expected BNP Values in Normal Individuals

The reference range data provided by the manufacturer of the Biosite BNP assay indicates that the most appropriate clinical decision threshold is 100 pg/mL. This value was obtained from the 95% confidence limit of BNP concentrations measured in a non-CHF population (age ≥ 55 ; n=1286; 676 female, 610 male). At this cut-off, the general specificity of the BNP test is >98%, i.e., less than 2% false positives were observed in patients without CHF. In interpreting BNP results, it is important to keep in mind that the imprecision (reproducibility) of the Biosite assay at this clinical decision limit is approx. 10%, i.e., the 95% confidence interval of a BNP result of 100 pg/mL is 80 – 120 pg/mL.

Clinical Applications of BNP: Sensitivity, Specificity and Predictive Value

1. Assessing Patients with Dyspnea in the Emergency Department

The main application of BNP is in assessing patients who present in the emergency department with dyspnea. The recently published results of the “Breathing Not Properly” study, a multi-center prospective clinical study (ref. 4) of 1586 patients who presented to the emergency department with

acute dyspnea as the most prominent symptom, showed the overall diagnostic accuracy of BNP measured at presentation using a clinical threshold of 100 pg/mL was 83.4% with a negative predictive value (NPV) of 89% and a positive predictive value (PPV) of 79% (sens.=90%, spec.=76%, prev.=47%) Lowering the BNP threshold to 50 ng/mL increased the NPV to 96% and raising the threshold to 150 pg/mL increased the PPV to 83%. A recently published flowchart describing a suggested diagnostic algorithm appears below.

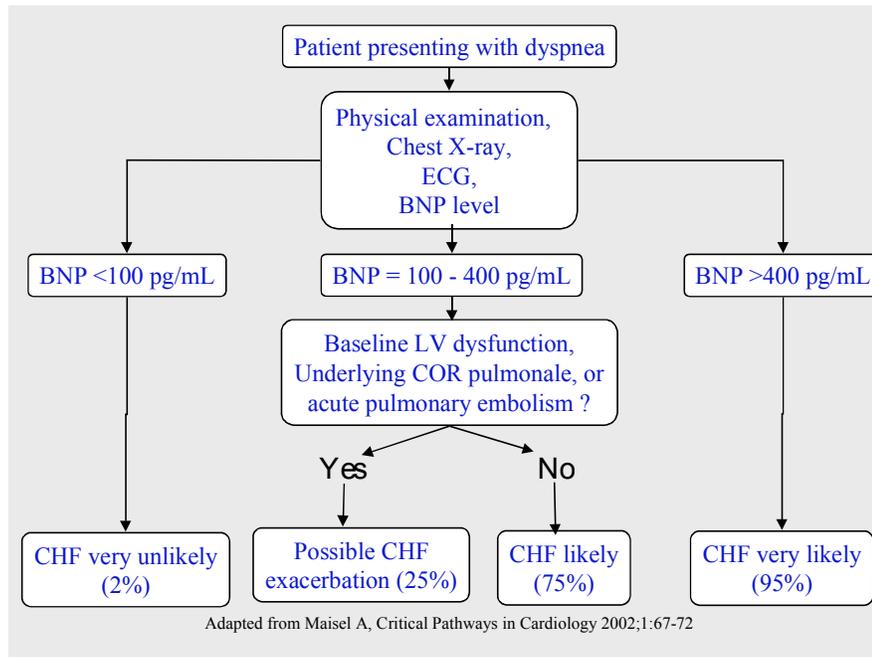
2. Assessing Known CHF Patients for Decompensated CHF

Another potential use of BNP measurements is in assessing known CHF patients who present with symptoms suggestive of decompensation to determine whether these symptoms are truly indicative of worsening CHF or are due to other causes. If the CHF patient's "baseline" BNP concentration of the patient is known, a recent recommendation by Maisel (ref. 5) suggests that true decompensation is likely if a 50% or greater increase in BNP vs. baseline is observed.

3. Monitoring Therapy in CHF Patients

The Biosite BNP assay has been approved by the FDA only for the diagnosis of CHF. The utility of this test to monitor the effectiveness of treatment for CHF is unproven and still under study.

Accordingly, there will be a limit of one BNP test per inpatient admission.



Questions? Questions may be referred to Dr. Salvador Sena (ext. 7622, pager #0109)

References

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4. Maisel AS, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. NEJM 2002;347:161-7.
5. Maisel A. Algorithms for using B-type natriuretic peptide in the diagnosis and management of congestive heart failure. Critical Pathways in Cardiology 2002;1:67-73.

