| **B-Type Natriuretic Peptide (BNP)** | |
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| **Purpose** | This procedure provides instructions for performing B-Type Natriuretic Peptide on the Abbott Architect. |
| **Policy Statements** | This procedure applies to all personnel responsible for performing testing on the Abbott Architect. |
| **Principle** | The ARCHITECT BNP assay is a two-step immunoassay for the quantitative determination of human B-type natriuretic peptide (BNP) in human EDTA plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex. Sample and anti-BNP coated paramagnetic microparticles are combined. The BNP present in the sample binds to the anti-BNP coated microparticles. After washing, anti-BNP acridinium-labeled conjugate is added to create a reaction mixture. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of BNP in the sample and the RLUs detected by the ARCHITECT iSystem optics. |
| **Clinical Significance** | Heart failure is a syndrome caused by a variety of conditions such as coronary artery disease, hypertension, valve disease, myocarditis and others. Common symptoms of heart failure include shortness of breath, coughing under exertion, swelling of appendages, and dizziness. Heart failure is better defined as the progressive inability of the heart ventricles to pump blood out to the lungs and/or the extremities. Heart failure is either systolic or diastolic or a combination of both. Severity is usually classified into four classes defined by the New York Heart Association (NYHA class I-IV).  BNP is one member of the family of natriuretic peptides that were initially discovered by de Bold, et al. Although BNP was first isolated from porcine brain tissue (originally named brain natriuretic peptide) the heart has been determined to be the major source. BNP is synthesized and released into the blood in response to volume overload or conditions that cause ventricular stretch, to control fluid and electrolyte homeostasis by interaction with the renin-angiotensinaldosterone system (RAAS). PreproBNP (134 amino acids) is synthesized in the cardiac myocytes and is processed to a proBNP (108 amino acids) precursor molecule. The proBNP is subsequently cleaved into physiologically active BNP (32 amino acids), and a degradation fragment NT-proBNP (76 amino acids). BNP, NTproBNP, and a higher molecular weight form have been detected in peripheral blood. BNP is cleared from the circulation, with a half-life of approximately 23 minutes, by specific cellular receptors and neutral endopeptidases.  Numerous studies have indicated that BNP can be used for patient diagnosis, prognosis and therapy monitoring. Levels of BNP have been shown to be elevated in patients with cardiac dysfunction. Plasma BNP levels provide clinically useful information concerning the diagnosis and management of left ventricular dysfunction and heart failure, which complements other diagnostic testing procedures (e.g., electrocardiograms, chest x-rays, and echocardiograms). BNP levels can be used to assess the severity of heart failure, as demonstrated by the correlation with New York Heart Association classifications. Plasma BNP levels also increase with decreasing physiological functional capacities, as measured by left ventricular ejection fraction (LVEF) or exercise based evaluations. The European Society of Cardiology has included the use of natriuretic peptides (e.g., BNP) testing in their guidelines for the diagnosis or rule out of heart failure. Others have suggested that BNP has utility in the stratification of patients with heart failure and acute coronary syndrome (ACS). Elevated levels of BNP in heart failure patients predict disease progression and increased morbidity and mortality. Studies also suggest ACS patients with increased BNP levels have a higher rate of cardiac complications and higher mortality post |
| **Clinical Significance (Continued)** | myocardial infarction. Preliminary studies have reported the use of BNP measurements to optimize patient treatment / management for heart failure. Nesiritide (Natrecor), recombinant BNP has been used for treatment in patients with acute, decompensated heart failure. The efficacy of BNP monitoring, pre- and post-treatment with Natrecor, has been studied. Measurements of BNP two hours or more post treatment detect only the endogenous levels of BNP. |
| **Instrument** | **PRIMARY METHOD: Abbott Architect i1000SR**  **SECONDARY (BACKUP) METHOD:**  **Minneapolis: Abbott Northwestern Hospital/Allina Central Laboratory**  **St. Paul: United Hospital Laboratory (Used also for STATs originating in St. Paul)** |
| **Sunquest Test Code** | **BNPT** |
| **Specimen** | **Sample type:** EDTA Plasma  **Minimum volume:** 200 µL of serum or plasma  **Stability:** 4 hours at room temperature, 24 hours at 2-8°C, 3 months at -20°C or colder.  **Rejection criteria:** Unlabeled specimens, incorrect sample type, grossly hemolyzed samples, samples collected in glass containers  **Shipping:** If testing will not occur within 24 hours of collection, freeze samples for transport; otherwise, ship and store refrigerated.  STAT samples originating in St Paul should be sent to United Hospital Laboratory.  **Preparation:**   1. Plasma specimens can be centrifuged immediately 2. Plasma should be physically separated from cells as soon as possible with a maximum limit of two hours from the time of collection. 3. Lipemic samples should be ultrafuged. 4. Specimens should be free of particulate matter. 5. Transfer plasma to a properly labeled sendout tube. Minimum labeling includes sample accession ID, and/ or patient name, medical record number, collection date and time. |
| **Reagents** | |  |  |  |  | | --- | --- | --- | --- | | ***Product Description*** | ***Product Code*** | ***Stability*** | | | BNP Reagent | 8K28 | **Store at:** 2 – 8 °C  **Unopened/Opened:** Manufacture expiration date.  **On-board:** 30 Days | | BNP Calibrator | 8K28-02 | **Store at:**  2-8°C  **Unopened**: Manufacture expiration date.  **Opened**: Store at 2 – 8 °C, stable until expiration date when stored and handled as directed. | | Multiassay Diluent | 7D82-50 | Refer to Supply Status on Analyzer | | Pre-Trigger Solution | 06E23-65 | Refer to Supply Status on Analyzer | | Trigger Solution | 06C55-60 | Refer to Supply Status on Analyzer | | Wash Buffer | 06C54-58 | Refer to Supply Status on Analyzer | | Reaction Vessels | 07C15 (-02 or -03) | N/A | |
| **Risk and Safety:** | Contains methylisothiazolones and sodium azide. Avoid contact with skin and eye. Causes serious eye irritation. Wear gloves. Contact with acids liberates very toxic gas. Recap and dispose of in appropriate Hazardous Waste Container. |
| Calibration/ Verification/AMR | |  |  | | --- | --- | | Analytical Measuring Range: | 10 - 5000 pg/mL | | Reference Material: | BNP Calibrator | | Suggested Calibration Levels | A – 0.0 pg/mL  B – 75.0 pg/mL  C – 375.0 pg/mL  D – 750.0 pg/mL  E – 2500.0 pg/mL  F – 5000.0 pg/mL | | Verification Scheme: | n=6 | | Verification Frequency: | * For each new lot of reagent * After major maintenance or service, if indicated by quality control results * As indicated in laboratory quality control procedures | | AMR | Verification of AMR is accomplished with each calibration.  Cal Verification and AMR verification are performed at least once every six (6) months with each calibration of reagent. | |  | | | |
| **Quality Control** | **Abbott Diagnostics BNP Controls**  **Frequency:** Three levels each day of use.  **Stability:** Until expiration date when stored at 2-8°C and handled as directed.  **Preparation**: May be used immediately after removal from refrigerated storage. Prior to use, mix by gentle inversion 5-10 times. After each use, tightly close the caps and return the controls to  2-8°C storage.  **Sunquest Control names:**  Abbott Diagnostics BNP Control L: **C-BNP1**  Abbott Diagnostics BNP Control M: **C-BNP2**  Abbott Diagnostics BNP Control H: **C-BNP3**  **Acceptable ranges:**   * Ranges are current in Sunquest and the instrument. Refer to the Quality Control in Chemistry procedure for QC exception codes. * If a control value is outside the confidence interval, the determination must be repeated. If the repeat determination confirms the deviation, a new reference curve should be established. * Do not release patient results until the cause of deviation has been identified and corrected * When a new lot of assayed control is received, validate the manufacturer’s insert range by running the new lot in parallel with the current lot, and confirming that the results obtained are within the stated range * When a new lot of unassayed control is received, verify new ranges by running the new lot in parallel with the current lot 20 times, and calculate a new range using the method mean ± 2 SD. Ranges are current in Sunquest and the instrument. Refer to the Quality Control Procedure for QC exception codes. |
| **Interferences** | * Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits which employ mouse monoclonal antibodies. ARCHITECT BNP reagents contain a component that reduces the effect of HAMA reactive specimens. Additional clinical or diagnosis information may be required to determine patient status. * Heterophilic antibodies in human plasma can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. The presence of heterophilic antibodies in a patient may cause anomalous values to be observed. * Measurements of BNP should occur prior to Nesiritide (Natrecor), recombinant BNP treatment, and 2 hours post-treatment. |
| **Reference Range** | Newborns, 0 to 7 days of age: <232 pg/mL  Male: <100 pg/mL Female (<75 yrs): <150 pg/mL Female (>75 yrs): <265 pg/mL |
| **Critical Values** | None specified |
| **Limitations** | The instrument reporting system contains error messages to warn the operator of specific malfunctions. Refer to Operator’s Manual for troubleshooting specific error messages. |
| **Dilutions** | Specimens with a BNP value exceeding 5000.0 pg/mL are flagged with the code “>5000.0” and may be diluted using the Automated Dilution Protocol. The system performs a 1:5 dilution of the specimen and automatically calculates the concentration of the specimen before dilution and reports the result. |
| **Result Reporting** | Results less than 10 are reported as <10 rather than a numerical value.  Results between 10 and 5000 are reported as the numerical value.  Results >5000 are repeated with automated dilution protocol and are reported with the numerical result up to 25,000. Results >25,000 are reported as such. |
| **Specimen Storage** | Promptly stopper tested specimen and store upright in specimen rack. Every 8 hours remove specimens to refrigerator/freezer storage. Samples are retained 14 days in Special Chemistry specimen storage freezer. |
| **References** | 1. Abbott Architect reagent cartridge insert sheet Abbott Laboratories, Abbott Park, IL, 60064. Revised Date November 2015. 2. Abbott Architect calibrator insert sheet Abbott Laboratories, Abbott Park, IL 60064. Revised October 2014. 3. Abbott Architect Safety Data Sheet, Abbott Diagnostics, Abbott Park, IL 60064. Revised 2016-04-09. 4. Abbott Architect BNP Controls Package Insert, Abbott Diagnostics, Abbott Park IL 60064. Revised December 2014. 5. Allina Health Laboratories, BNP reference intervals, accessed 8/20/2018. <https://ww5.allinahealth.org/ahs/allinalabs.nsf/ad88a4dd4aa66fe086256a47004f30e8/80fb384aeee41e1786256c6b008128bc?OpenDocument> 6. Koch, A., Singer, H. (2003, February 23.) Normal values of B-type natriuretic peptide in infants, children, and adolescents. Heart journal. 89:875-878 |
| **Historical Record** | |  |  |  |  | | --- | --- | --- | --- | | **Version** | **Written/Revised By** | **Effective Date** | **Summary of Revisions** | | 1 | Kelsi Brown/Erin Bartos | 8/22/2018 | New Procedure | |  |  |  |  | |  |  |  |  | |