Clinical Use

- Differentiate inherited NDI from acquired NDI
- Screen for autosomal NDI carrier status in at-risk individuals

Reference Range

Negative (no mutations detected)

Interpretive Information

Mutation present

- Nephrogenic diabetes insipidus (affected or carrier)

Clinical Background

Nephrogenic diabetes insipidus (NDI) is characterized by inability of the kidneys to concentrate urine despite the presence of arginine vasopressin (AVP), also known as antidiuretic hormone (ADH). This insensitivity to AVP results in polyuria, polydipsia, low urinary specific gravity, and high risk of severe dehydration, especially in affected infants.

Although acquired NDI is more common than inherited disease, genetic forms also occur. They can be transmitted in X-linked recessive, autosomal recessive, or autosomal dominant patterns. X-linked NDI, caused by mutations in the AVPR2, is the most common genetic cause of NDI. Most cases of autosomal NDI have a recessive mode of inheritance, but about 10% of them (1% of all inherited NDI) result from mutations with dominant expression.

Insertion of the aquaporin 2 (AQP2) protein into the luminal membrane of collecting duct cells is the final step in the antidiuretic action of AVP, providing specific channels that increase water permeability of the membrane. Mutations disrupting the AQP2 gene on chromosome 12 alter the amino acid sequence of the AQP2 protein and cause about 10% of familial NDI. Since about 25 different mutations have been identified in the AQP2 gene, gene sequencing is the method of choice for detecting AQP2 mutations. After identification of a mutation in an affected individual, genetic testing can be used to evaluate other family members.

Method

- Polymerase chain reaction (PCR) and DNA sequencing
- Analytical specificity: mutations in 4 exons of the AQP2 gene

Specimen Requirements

5 mL room temperature whole blood
3 mL minimum

Collect blood in a lavender-top (EDTA) or yellow-top (ACD solution B) tube.