

Title: Sweat Testing in CF Newborns Detected by Screening

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Synopsis:

The advantages provided by early diagnosis of cystic fibrosis were well recognized for many decades. This fact, along with the development of immunoreactive trypsinogen (IRT) determination in dried blood spots, led to the development of newborn screening strategies for CF. The data accumulated from a randomized controlled study of CF NBS, as well as longitudinal data collected from non-randomized studies, proved the benefits of early diagnosis prompted by newborn screening. However, NBS only identifies newborns at risk for CF and the benefits can only be fully realized when the appropriate follow up systems are in place, including the necessary confirmatory diagnostic testing as well as genetic counseling services. In California, newborn screening for cystic fibrosis started in July of 2007. The screening algorithm implemented starts with assaying the dried blood spot specimens for IRT. Blood spots from hypertrypsinogenemic infants are subsequently tested with a panel of CFTR mutations known to occur with increased frequency in California. Those infants with two mutations detected are identified as likely affected and referred to CF Centers for further confirmatory testing and evaluation. Those with only one mutation detected on the panel have their blood spot subsequently tested by focused DNA sequencing. This method can detect previously known as well as novel CFTR mutations and variants. Infants with two mutations/variants detected are then referred to CF Centers for further evaluation.

The California NBS algorithm will identify newborns carrying a wide spectrum of CFTR mutations and with corresponding varying degrees of CFTR dysfunction. This will likely include some infants with mild variants and thus only at risk for CFTR associated diseases. In this context, and taken into account the known potential pitfalls in sweat testing and result interpretation, it becomes of great importance to have a uniform protocol for sweat testing that includes patient preparation and assessment of fluid and electrolyte balance. This also provides a unique opportunity to evaluate the effect that fluid and electrolyte status has on sweat electrolytes in the presence of varying degrees of CFTR dysfunction. Further, this cohort of patients could provide important information on the longitudinal changes in these parameters over time, particularly those infants that have some level of CFTR function preserved. In a well defined cohort of newborns with known CFTR mutations, we aim to evaluate a uniform patient preparation protocol for sweat testing that includes salt supplementation and adequate fluid intake guidelines, determine the effect on sweat electrolytes of fluid and electrolyte status and assess for longitudinal changes in sweat electrolyte concentration and other clinical and laboratory parameters.