Population Based Newborn Screening for Rare Diseases

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Over 45 years ago, population based newborn screening was begun in the United States for the rare condition, phenyketonuria. Untreated persons with this condition had been known since the 1930s and had been found to have profound retardation, with IQs under 25. It had been discovered that a special dietary treatment, if begun in early infancy, would lead to essentially normal development. And importantly, a simple test, performed on a dried blood spot, could reliably and inexpensively be performed on the entire newborn population. This was done with a single punch from a single dried blood spot. Other diseases were soon recognized which benefited from newborn screening and treatment, and some states used this one-punch, one disease technology to screen for up to 10 individual diseases.

Technology changed dramatically in the 1990s with the introduction of tandem mass spectroscopy (M/MS) which permitted the accurate determination of over 40 conditions on a single punch from the dried-blood spot. Since that time there has been a rapid increase in the number of conditions for which infants are screened in the United States, and the benefits to specific infants, in the saving of lives, and the reduction of morbidity has been enormous.

Currently, national recommendations are that all infants (there are 4.1 million births each year in the US) be screened for 29 "core" conditions. These have been identified as being appropriate in that the conditions have a reliable screening tool, are very serious and would not otherwise be recognized in infancy, and there is a treatment which is beneficial. Newborn screening, the most common form of genetic testing is unusual in that this testing takes place in the public health system, under the aegis of the individual states. Although individual states decide what to screen for, at the current time about 90% of all babies born in the US are screened for these recommended conditions.

Newborn screening is also unusual in that you identify a "permanent disability", i.e. an abnormal protein or a deficiency of an enzyme which persists throughout one's life. However, with early identification and proper treatment, morbidity can be reduced greatly. PKU has already been discussed, but 33 states are currently screening for cystic fibrosis, 7 states have mandated but not yet begun such screening, and 2 states do it on request. These infants are accurately diagnosed with cystic fibrosis by genetic technologies, and some of their problems can certainly be addressed.

Virtually all states are offering newborn screening for hearing problems, and the degree and type of hearing loss can be accurately determined early in life. Importantly, interventions can be performed which improve the outcomes of these children.

There is dramatic new technology being developed for newborn screening. Current pilot projects are using microchip and bead based technology, and there are studies underway using nanotechnologies, a very exciting new development.

In addition to new technologies, there are new conditions for which newborn screening is being proposed. There are pilot projects underway to screen for Krabbe Disease and Pompe Disease. These can be accurately diagnosed and there are treatments available; however these treatments will not be curative. There will likely be significant problems which persist.

There are also discussions surrounding screening for genetic conditions which produce severe developmental delay, and for which there is not specific treatment. The best example is the most common genetic cause of mental retardation, the Fragile X syndrome, which will produce severe developmental delay, but will benefit from early intervention in childhood. Among other discussions are technologies to diagnose congenital heart disease.

Because of the extraordinary scope of newborn screening, the technologies used must be very accurate and also have standardized outcomes. Much effort if going into both of these areas. In addition, the long-term outcomes of these screened-positive infants will be a significant focus of planned NIH studies.