Data show a decline in cystic fibrosis since introduction of prenatal carrier screening

February 28 2008

A brief report in the February 28, 2008, *New England Journal of Medicine*, led by researchers at the New England Newborn Screening Program (NENSP) of the University of Massachusetts Medical School (UMMS), indicates a declining incidence of a genetic disease, providing what may be the first demonstration of a link between two independent population-based screening programs.

The state of Massachusetts has offered universal newborn screening to detect cystic fibrosis (CF) since 1999. Independently, recommendations for nationwide (adult) carrier screening for CF were introduced in the U.S. around 2002, coming from the National Institutes of Health, the American College of Obstetrics and Gynecology and the American College of Medical Genetics.

Newborn screening for cystic fibrosis (much like newborn screening for other conditions), a public health service geared toward improving the lives of babies born with treatable conditions, identifies infants across the state who are at risk for disease and ensures that these infants are referred for diagnostic evaluation and (when appropriate) care. Tracking the number of infants who are diagnosed with the disease is an integral part of quality assurance of the newborn screening program.

Using the Massachusetts newborn screening data, the researchers compared two four-year periods: 1999 to 2002, just before prenatal CF carrier screening came into wide practice, and 2003 to 2006.

The number of live-born infants with CF dropped by about 50 percent from one four-year period to the next. Moreover, among the babies who were born with CF, markedly fewer had two copies of the delta F508 gene mutation, associated with a severe form of CF. The authors, who work closely with the clinician directors of the five Massachusetts CF Centers at Baystate Medical Center in Springfield; Children's Hospital Boston; Massachusetts General Hospital; New England Medical Center; UMass Memorial Health Care in Worcester; and UMMS, are confident that the decrease is real—not an aberration of the screening program and not a normal fluctuation.

Clinical researchers have understood that a major challenge of CF newborn screening is developing treatments to maintain the health of relatively asymptomatic newborns. "Our recent observations that fewer infants are being born with CF—particularly fewer infants with a severe genotype—provides an additional challenge to researchers developing new treatments or using population data for trend analyses," says Anne Comeau, PhD, associate professor of pediatrics at the University of Massachusetts Medical School and deputy director of the NENSP. "We should not fool ourselves into thinking that our treatments are working better than they are if the treatment may be tested on a population that was already bound to be more healthy."

The authors hypothesize that the gradual implementation of the recommendation to offer preconception and prenatal screening in order to identify carriers of CF might have yielded a decrease in the number of births of infants with CF, particularly the type that causes the most severe disease.

"Our data cannot distinguish the reason for the reported decrease," notes Richard Parad, MD, MPH, a newborn medicine specialist at Children's Hospital Boston and Brigham and Womens Hospital, who co-authored the study with Jaime Hale of NENSP and Comeau. "Carrier couples may

have chosen not to conceive, or they may have resorted to donor egg or sperm or to pre-implantation genetic diagnosis, or they may have decided to terminate affected pregnancies."

CF affects all races, and is the most common autosomal recessively inherited disorder in Caucasians (about 1/3000 births). Fifty years ago, most children with CF died before they reached school age, but today, with early diagnosis and improved treatment, the median survival is 36 years.

Source: University of Massachusetts Medical School