Medscape Medical News

Tandem Mass Spectrometry Improves Newborn Screening: A Newsmaker Interview With Piero Rinaldo, MD, PhD

Laurie Barclay, MD

Feb. 23, 2005 — Editor's Note: Tandem mass spectrometry can be used to effectively screen newborns for more than 40 potentially life-threatening novel inborn errors of metabolism with informative amino acid and/or acylcarnitine profiles, according to a presentation on Feb. 21 at the annual meeting of the American Association for the Advancement of Science in Washington, D.C.

This screening method, which combines state-of-the-art technology and double-tiered analysis, could improve genetic screening for newborns nearly 40-fold. However, inconsistent implementation at the state level prevents early diagnosis and life-saving intervention for many infants.

To learn more about the ramifications of this screening program, Medscape's Laurie Barclay interviewed presenter Piero Rinaldo, MD, PhD, a pediatric geneticist at the Biochemical Genetics Laboratory of the Mayo Clinic College of Medicine in Rochester, Minnesota. Dr. Rinaldo's presentation was part of a symposium titled "The Future of Newborn Screening: Science, Policy and Technology," organized by a panel from the National Institute of Childhood Diseases and the University of Miami School of Medicine.

Medscape: Please explain how the Minnesota method of newborn screening with tandem mass spectrometry works and which diseases it is able to diagnose.

Dr. Rinaldo: Since June 2004, we have established a public-private partnership between the Minnesota Department of Health (MDH), the University of Minnesota, and the Mayo Clinic. The main components of our model are the transfer of the analytical testing by tandem mass spectrometry to Mayo (we have a lot of experience in the diagnostic arena for the same conditions targeted by the screening program), the reliance on second-tier tests to minimize the false-positive rate, and the focus on communication and cooperation between all the parties involved. We talk constantly; we have a secure Web site for posting of results.

Medscape: What are the advantages of early diagnosis of genetic conditions?

Dr. Rinaldo: First, prevention of morbidity and mortality, with the understanding that a less-than-perfect outcome is still a clear benefit to the affected newborn. Second, avoidance of extreme cases of "medical odyssey," when it takes months, and hundreds of

thousands of dollars, to make a diagnosis; and third, benefits of early identification, particularly offering to parents the option of family planning and reproductive choices as they deem appropriate.

Medscape: How sensitive and specific is the Minnesota method in detecting various genetic conditions?

Dr. Rinaldo: Analytically, we don't do things much differently from other public and private providers of the same services. If there is a difference, probably it can be found in the expertise we apply at the postanalytical level, meaning the interpretation of results and the ability to pick up subtle changes and sort out those that are clinically significant from others that are not. In 2004, our detection rate was 1:2,089 — elsewhere you see numbers as high as 1:15,000. The false-positive rate from June to December was 0.12%. It's not rare [elsewhere] to see it as high as 0.80%; the worst I have seen is 3.0%.

Medscape: Please address issues of lack of uniformity and fairness in applying tandem mass spectrometry and how these might be best resolved.

Dr. Rinaldo: Many states are still not offering screening by tandem mass spectrometry. In some cases, even within the same state, [infants in] some areas and hospitals are being tested, while others are not. This happens right now, for example, in Utah, California, and Florida. How would you feel if your child dies of a disease and after the fact you are told that he or she would have been picked up and probably be alive and well if born not even in a neighboring state but just in the next county?

Medscape: How cost-effective is the Minnesota method?

Dr. Rinaldo: I have data for congenital adrenal hyperplasia [CAH]: if a baby born here at Mayo has an abnormal primary screening test, the overall cost of evaluation, with clinical examination and lab tests, is approximately $847. The second-tier test costs $35 and eliminates about 80% of the false-positive tests. So, the cost of follow-up for 100 cases could be as low as $3,500 instead of $84,700 (less than 5%). This is now a pretty controversial issue. Indeed, there are folks who argue against this, claiming that there is a better way to do it: if they have a first abnormal result, they collect a second blood spot and repeat the same test, but if the test is normal, they call the whole thing off. A repeat test costs less than the second-tier test.

However, I am beginning to wonder why the 10-year (1990-1999) detection rate of CAH by screening is 1:19,000, and in eight months we have seen 1:6,000. Perhaps, just perhaps, the other approach not only has poor specificity but is also not as sensitive as believed to be, and true positives, especially cases of nonclassical CAH, are ruled negative when they should not have been.

Medscape: How widespread is the use of tandem mass spectrometry currently, what are the barriers to wider use, and how widespread do you believe it could ultimately become?

Dr. Rinaldo: Right now there is a lot of activity in California, New York, Florida, and other states, mostly in response to the uniform panel proposed by the American College of Medical Genetics/Health Resources and Service Administration expert panel. Securing the political will to do it is the necessary first step; what happens afterward is really about the ability, or lack of, to do the testing properly. I am confident that the goals of universality and uniformity are achievable in the U.S., but it is hard to tell how long that is going to take.

However, the situation is reaching the point where legal liability could become a real issue for physicians and hospitals located in states reluctant to upgrade their programs. States, as you may know, have legal immunity, but docs don't, and they had better wake up and understand they are likely targets of future malpractice lawsuits, as in, "You didn't tell me it's possible to screen for more of what our state is doing." This has become a hot issue since last year the feds told states they had better inform the public of the option to have more testing done. My reason to call it lack of fairness is driven in part by the reality of screening left to the discretion of the consumer!

Medscape: If tandem mass spectrometry were widely implemented, what effect do you believe it would have for newborns diagnosed with specific conditions and for public health in general?

Dr. Rinaldo: Again, early intervention and identification are key preventive measures. Sadly, preventing just two or three catastrophic episodes, for example, of very long chain fatty acid dehydrogenase deficiency, is all that is needed to support an average program for a full year. The choice is to pay $30 to $50 one baby at a time or $400,000 just once, and for only one of them. I hate to trivialize this to money, [but] that at times seems to be the only argument that gets the proper attention.

Presented at the AAAS 2005 Annual Meeting.
Curr Opin Pediatr. 2004;16(4):427-433

Reviewed by Gary D. Vogin, MD

Betty Connal
Executive Director
SIDS Mid-Atlantic
2700 S. Quincy St suite 220
Arlington VA 22206
703-933-9100
www.sidsma.org
cfc 6014
cvc 3392