



E' SEMPRE CORRETTO CHE IL NEONATO DIVENTI PAZIENTE? COSA HA CAMBIATO LO SCREENING ESTESO PER LE MALATTIE METABOLICHE?

P. Rinaldo

Biochemical Genetics Laboratory, Mayo Clinic College of Medicine, Rochester, MN, USA

Tandem mass spectrometry (MS/MS) allows for the rapid analysis of individual compounds in complex mixtures, and provides an excellent analytical methodology for newborn screening. The extent and complexity of newborn screening by MS/MS have triggered some controversy, particularly over the distinction made between primary and secondary targets in recent recommendations [Genet Med 2006;8(Suppl 1):1S-252S]. Opposition to the implementation of the recommended panel is likely the combination of limited technical knowledge and a failure to appreciate the need to provide a differential diagnosis between primary and secondary conditions presenting with abnormal concentrations of the same marker(s). If conditions were to be removed from the list of secondary targets on the sole basis of not requiring a differential diagnosis from a primary condition, only argininemia and 2,4 dienoil-CoA reductase deficiency would be candidates for exclusion from the panel.

On the other hand, too much emphasis has been placed on the "quantity race" (i.e. who screens for more conditions must have the best program), even leading to representation of excellence on the sole basis of the number of conditions tested by a given state. It is concerning that so little attention has been given to the issue of quality assessment and improvement, defined here broadly as the longitudinal monitoring and specifically inter-laboratory comparison of performance metrics in newborn screening testing. The expansion of newborn screening programs to include multiplex testing by MS/MS requires clinically validated cutoff values and close monitoring of performance metrics. Between July 2004 and April 2006 (N=176,185 cases), the overall performance metrics of the Minnesota program were as follows: detection rate 1:1,186, positive predictive value 37%, and false positive rate 0.09%. These metrics are the cumulative result of many factors, including the implementation of second tier tests for most common abnormalities seen in the primary screening, and reliance on tools derived from a multi-center collaborative database of true positive cases (N=1,579 as of June 1, 2006). This database is the source of evidence for harmonization of clinically driven cut-off values between the 99%ile of the normal population and the 5%ile of the disease range.