

## Plenary Abstract

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### Newborn Screening: Are We Ready for It?

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#### BACKGROUND

The newborn screening (NBS) programme is a complex and organised system consisting of family and personal education, biochemical tests, confirmatory biochemical and genetic tests, diagnosis, therapy, and patient follow-up. The programme identifies treatable metabolic disorders, possibly when still asymptomatic, by using dried blood spot (DBS). Over the last 20 years, tandem mass spectrometry (TMS) has become the leading technology in NBS programmes and has been shown to be versatile, sensitive and specific. There is consistent evidence of benefits from NBS for many disorders detected by TMS as well as for congenital hypothyroidism, cystic fibrosis and congenital adrenal hyperplasia by immune-enzymatic methods. Some methods were developed for the detection of lysosomal storage disorders (LSDs), and even if for some of them there is a reliable and relatively simple test, a reasonable associated therapy may still not be available. Therefore the inclusion of LSDs in NBS is still under debate.

#### MATERIALS AND METHODS

At the beginning of the 2000's, fluorometric methods were developed for many LSDs such as Pompe disease, Gaucher disease, Fabry disease, mucopolysaccharidosis (MPS), Hurler-like LSDs, Niemann-Pick A/B disease, Tay-Sachs disease and Sandhoff disease. However, the incorporation of a chromophore or fluorophore into the substrate caused false-negative results and had the limitations of specificity and limited capacity for multiplexing. In recent years new

MS-based technology for simultaneous screening of several enzyme activities related to lysosomal storage disorders from DBS was developed, replacing the old methods and enabling the assay of single enzyme activity. Li et al (1) first developed a direct multiplex assay of lysosomal enzymes for Gaucher, Pompe, Krabbe, Fabry and Niemann-Pick A/B diseases in DBS by flow injection analysis (FIA) tandem mass spectrometry. Since then, an expansion of simultaneously diagnosable disorders by MS has been reported. Some countries already include some LSDs in their newborn screening panels, and local or pilot programmes have been launched in others. (2-6).

#### CONCLUSIONS

It is currently debated whether or not LSD diseases should be included in a general NBS worldwide programme. In 2014, most LDS pilot projects include Pompe disease. In general, NBS for LSD could identify asymptomatic forms; it is not able to discriminate between treatable and untreatable forms, surely it cannot suggest if and when to start therapy. However, even if long-term clinical studies are not available, it seems that Pompe disease meets the criteria for inclusion in NBS, including basal availability of a simple test, a combination therapy that modifies the natural course of the disease, and early diagnosis that allows for genetic counselling and prenatal diagnosis in families with an affected baby.

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