

Recommendations for the expansion of newborn screening to MCAD* deficiency

June 2011

These recommendations are in line with the National Plan on Rare Diseases 2010-2014 (measure A-1-6). Their primary target audience are public health policy makers but they are also meant for health professionals and patients' organizations concerned with newborn screening and with managing the disorders that can be detected through this screening.

MCAD deficiency is an inherited metabolic disorder characterised by the inability of the body to use fat. While children with MCAD do not have symptoms at birth, they may develop a metabolic crisis (e.g. during intercurrent illness), which may rapidly lead to coma or death.

The long-term management of MCAD deficiency consists of dietary measures aimed at preventing fasting episodes and increasing carbohydrate intake during periods of high energetic needs. When it is introduced early, this preventive treatment reduces the morbidity and mortality to virtually nil.

Key messages

HAS recommends the expansion of newborn screening to MCAD deficiency in the general population.

- This screening is based on the technology of tandem mass spectrometry, using Guthrie cards.
- The introduction of this technology implies a reduction in the number of labs that are performing newborn screening tests, in order to guarantee the quality of the technical expertise and to achieve efficiency.
- The implementation of this screening calls for the training of health care staff and for the development of appropriate informational materials, as well as for the establishment of a system for monitoring and evaluating newborn screening.

* Medium chain acyl-CoA dehydrogenase.

BACKGROUND AND OBJECTIVE

Newborn screening is a public health intervention aimed at detecting at birth certain severe diseases, mostly of genetic origin, and to implement, before the onset of symptoms, a treatment or another form of appropriate disease management to prevent or to reduce mortality and morbidity.

In France, 5 diseases are currently subject to newborn screening using biological tests on dried blood spots (Guthrie card): phenylketonuria, congenital adrenal hyperplasia, congenital hypothyroidism, sickle cell disease, and cystic fibrosis.

These recommendations for the expansion of newborn screening to include MCAD deficiency are based on an a priori evaluation of the expansion of newborn screening to one or more inborn error(s) of metabolism using the technology of tandem mass spectrometry (MS/MS).

They subscribe to the prospect of improving the health of the populations (decreasing mortality and morbidity), reducing health inequalities, and rationalizing the use of resources and improving health practices.

INBORN ERRORS OF METABOLISM TO BE SCREENED

1. HAS recommends to expand newborn screening to MCAD deficiency in the general population in France. This screening necessarily implies the use of the technology of tandem mass spectrometry (MS/MS).
2. Corollary, for efficiency reasons, HAS recommends at the same time a shift to the MS/MS technology for newborn screening of phenylketonuria (PKU).
3. HAS stresses that the expansion of newborn screening to other inborn errors of metabolism using MS/MS would require an evaluation of the clinical utility and the ethical legitimacy of screening each of these conditions.

IMPLEMENTATION

4. With the objective of expertise acquisition and maintenance and of efficiency, HAS recommends that the clinical labs equipped with MS/MS for newborn screening activities should perform a minimum of around 50 000 tests per year.
5. This threshold calls for a reduction in the number of labs in charge of newborn screening (currently 22), which should be comprised between 5 and 15 labs equipped with MS/MS. Consequently, HAS indicates that it is likely to be inefficient to maintain the existing network of 22 labs in charge of newborn screening for diseases that are not detectable by MS/MS. Consequently, HAS recommends that all newborn screening tests should be performed in the 5 to 15 labs equipped with MS/MS.
6. HAS recommends that the criteria guiding the choice of the labs equipped with MS/MS be:
 - Demographic criteria;
 - Existing expertise;
 - Inter-regional collaboration networks.

7. Given the potential impact of such a reorganisation, HAS recommends that the expansion of newborn screening to MCAD deficiency and the shift to MS/MS technology for the screening of PKU should be roll out progressively, starting with one or two inter-regions to ensure a step by step, smooth implementation.
8. HAS recommends the use of a validated MCAD deficiency and PKU screening algorithm and of a standardized guideline for the management of patients detected with MCAD deficiency.
9. The implementation of this newborn screening will have to rely on existing structures. HAS recommends that specific guidelines for the management and follow-up of patients with MCAD should be developed in collaboration with reference centres.
10. HAS recommends that the expansion of newborn screening should be accompanied by training of all health professionals involved in newborn screening. This training should include both technical and human relation aspects, in particular with regards to the delivery of information.
11. HAS recommends that information should be given to the parents a first time during pregnancy, at the time of third trimester antenatal visits.
12. HAS recommends that appropriate informational material should be developed and targeted towards different audiences including parents and future parents, health professionals involved in newborn screening and in management of patients detected through screening, patients and their families, as well as the public at large.

MONITORING AND EVALUATION

13. HAS recommends that a quality assurance system aimed at evaluating the performances and improving the quality of the different components of the newborn screening programme (information, lab, diagnostic, management and follow-up) should be set up.
14. HAS recommends that a monitoring and evaluation system should be put in place, which would allow the evaluation of the structure, the process, the results and the impact of the newborn screening programme. HAS highlights in particular the importance of evaluating the long-term impacts of the newborn screening programme.
15. HAS recommends the use of the following indicators (minimum, not exhaustive list):
 - participation rate;
 - recall rate for abnormal results;
 - prevalence (and mutations frequency);
 - positive predictive value;
 - false negative rate;
 - time to referra;
 - follow-up rate;
 - clinical results (clinical evolution, complications, death).
16. HAS recommends that a discussion should be initiated on the conservation and potential use of dried blood spots (Guthrie cards) in a way that guarantees the privacy of patients and their families.

Perspectives

The 2nd part of HAS' work will evaluate the expansion of newborn screening to other inborn errors of metabolism using the technology of tandem mass spectrometry.

Key figures

- The prevalence of MCAD deficiency at birth ranges between 1/8 000 and 1/25 000 in different European countries; it is not precisely known in France.
- In the absence of screening, two thirds to three quarters of patients with MCAD develop a metabolic crisis which will lead to death in 20% of the cases and to neurological sequelae in 10%.
- Data from newborn screening programmes outside France indicates that the mortality due to MCAD deficiency is four-fold lower among screened children.
- Modelling the expansion of newborn screening to MCAD deficiency combined with a shift in technology (to MS/MS) for PKU screening in France suggests that such screening will prevent each year 5 deaths and the occurrence of neurological sequelae in 2 children under 5 years of age, with a incremental cost-effectiveness ratio below 10 000 € per life year and per quality adjusted life-year (QALY) gained.



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These recommendations, as well as the scientific argumentation, are available (in French) in their entirety on www.has-sante.fr