Review

Neonatal Mass Screening for Metabolic Disorders

Summary of Recent Sessions of the Committee of Experts to Study Inborn Metabolic Diseases, Public Health Committee, Council of Europe


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Abstract. The present situation of neonatal mass screening for metabolic disorders in eleven European countries is presented. The only disease screened for on a population wide basis in almost all countries is phenylketonuria. Screening for congenital hypothyroidism has been started in most countries or is under active consideration. A priority list of disorders that should be screened for routinely in all newborns comprises congenital hypothyroidism, hyperphenylalaninaemia, galactosaemia and maple syrup urine disease. Other disorders, like adrenogenital syndrome, cystic fibrosis, Duchenne's muscular dystrophy, histidinaemia, or tyrosinaemia cannot be recommended for mass screening at present because of an unsatisfactory test procedure or lack of effective treatment.

Key words: Screening - Neonatal mass screening - Metabolic disorders - Hypothyroidism - Hyperphenylalaninaemia - Galactosaemia - Maple syrup urine disease - Adrenogenital syndrome - Cystic fibrosis - Duchenne's muscular dystrophy - Histidinaemia - Hypermethioninaemia - Tyrosinaemia - Haemoglobinopathies - Glucose-6-phosphate dehydrogenase deficiency

Following the invitation of the Public Health Committee of the Council of Europe, a group of scientists representing the different countries—Committee of Experts to study Inborn Metabolic Diseases—met in Straßbourg in February and November, 1980 to take stock of the present situation regarding neonatal mass screening for metabolic disorders in the various countries and to give recommendations for such screening programmes in the light of new developments since the last meeting of this group in 1972.

In the following a summary of the committee's report will be presented.

Screening activities in the various countries are summarized in Table 1. More details about screening results are given in the appendix, Tables 4–7.

Neonatal mass screening for metabolic disorders is understood to mean an unselective programme routinely used on every newborn infant in the community. It concerns diseases which are treatable, are not easily recognized by clinical means during the neonatal period, and need immediate therapy to prevent irreversible disabilities. Other goals of neonatal screening—such as genetic counselling or enumeration and research—were thought not to justify routine mass screening, but can well be the purpose of selective research screening programmes.

Metabolic disorders under consideration for neonatal mass screening are listed in Table 2. Part I contains diseases in order of priority which should be routinely screened for on a population-wide basis, whereas in part II those diseases are listed for which mass screening can not be recommended at present. Tests available for mass screening for the different metabolic diseases are given in Table 3. In relation to new developments the various disorders will be discussed in the order given in Table 2 (for references and further details see Bickel et al. [1]).
Table 1. National mass screening activities (date: December 1979)

<table>
<thead>
<tr>
<th>Country</th>
<th>Hypothyroidism</th>
<th>Hyperphenylalaninaemia</th>
<th>Galactosaemia</th>
<th>MSUD</th>
<th>Hypermethioninaemia</th>
<th>Histidinaemia</th>
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</table>

+ = Screening done nationwide, covering more than 90% of the newborn population
(+)= Partial screening, not offered by all screening centres
- = Screening not done

Table 2. List of metabolic disorders under consideration for newborn screening

I. Recommended for mass screening (in order of priority)
   Hypothyroidism
   Hyperphenylalaninaemia
   Galactosaemia
   Maple syrup urine disease (MSUD)
II. Mass screening not recommended at present. Selective screening or research screening already performed or under discussion (in alphabetical order, not in order of priority)
   Adrenogenital syndrome (AGS)
   Amino acid disorders: urine screening
   Cystic fibrosis
   Duchenne's muscular dystrophy
   Glucose-6-phosphate dehydrogenase deficiency
   Haemoglobinopathies
   Histidinaemia
   Hypermethioninaemia
   Tyrosinaemia

Hypothyroidism

Hypothyroidism ranks first in neonatal screening because of its frequency (more than 1:4000) and the ease and efficiency of its treatment. Screening for this disease is already being done in most countries or is under active consideration in the others.

Screening should be based on the assay of thyroid stimulating hormone (TSH) rather than thyroxine (T4) because of the low recall rate. It is recognised that patients with low TSH due to secondary hypothyroidism accounting for less than 5% of all cases will not be detected. However, these patients do not appear to develop severe mental subnormality. It is strongly recommended that the screening programmes should be closely linked with those for hyperphenylalaninaemia and that personnel experienced in radioimmunoassay is necessary in the laboratory work. Quality assurance is essential.

According to the most recent WHO recommendation, TSH standards in dried blood filter paper specimens should be developed and used in all programmes.

Recommendations for the evaluation and therapy have been given in the International Conference on Neonatal Thyroid Screening, Quebec, 17–19 September 1979 [2].

Although screening for hypothyroidism is more expensive than screening for aminoacidopathies, it still has a positive cost/benefit ratio. The cost for testing one newborn infant for TSH (including staff, reagents and overheads) in Switzerland has been calculated to be approximately 5 Swiss Francs [3].

Hyperphenylalaninaemia

Since 1972 the difficulty in differentiating classical phenylketonuria from milder forms of hyperphenylalaninaemia has become obvious. Phenylalanine metabolism shows genetic heterogeneity, including variation in the activity of phenylalanine hydroxylase and enzyme defects of the biopterin pathway. The term "hyperphenylalaninaemia" covers this wide spectrum