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Chromatographic screening of 70,328 neonates for inborn errors of amino acid metabolism

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Between the years 1974 and 1984, amino acid chromatography was performed from dried blood spots and partly from urine of 70 328 neonates. Six cases of phenylketonuria, one histidinaemia, one hyperglycinaemia and three cystinurias were found. Since all these could have been detected by other methods, the regional screening was discontinued in agreement with international recommendations.

The enthusiasm elicited by the first results of neonatal mass screening for phenylketonuria (PKU) in the early sixties animated to the early detection of as many inborn errors of amino acid metabolism as possible [6]. This tendency was promoted by the elaboration of simple screening methods including a variety of chromatographic procedures from dried blood or urine spots [1, 7, 13, 14, 15, 16].

In accordance with the international trend, we also introduced a regional neonatal amino acid screening; its results are presented here.

Material and Methods

From January 1, 1974, to April 30, 1984, capillary blood samples dried on filter paper were collected from the liveborn neonates in the 5 obstetrical units of county Győr-Sopron (North-West Hungary). In the first two years of the programme urine samples were also obtained, from 1976 only blood spots were examined. The materials were taken on the 5th or 6th day of life, and the filter papers were sent to our laboratory.

Here two-dimensional thin-layer amino acid chromatography was performed according to White [16]. When the result was equivocal, the procedure was repeated from another disk of the original filter paper. If the finding was still uncertain or pathological, the infant was called to our department where fresh blood and urine samples were taken, the child was thoroughly examined, and hospitalized, if necessary. In these cases quantitative amino acid concentrations were determined with a Beckman Multichrom 4225 column analyser.

From January 1, 1975, parallel blood samples were analysed in the frame of the nationwide screening for PKU by means of Guthrie's bacterial inhibition test.

Results

A total of 70,328 newborn infants were screened. This covered 95.5% of all the liveborn neonates of the region in the given period.

In 1158 cases, i.e. in 1.65%, the chromatography had to be repeated, mainly because of insufficient separation of the individual amino acid spots. Only 79 infants, i.e. 0.11% of the whole material, had to be recalled for further investigation.

In 11 infants, some inborn error of amino acid metabolism could be verified with the following distribution:

PKU	6
Histidinaemia	1
Ketotic hyperglycinaemia (propionic acidaemia)	1
Cystinuria	3

Discussion

In the first years of our screening programme this organisation proved to be undoubtedly useful. It contributed to the high efficiency of the nationwide PKU + galactosaemia screening, and obviously helped to prepare the introduction of regional hypothyroidism screening in Hungary [10].

Having gathered more experience, it became evident that mass screening for all amino acid disorders was not rentable. In contrast to several surveys applying different methods, no aminoacidopathies other than PKU were discovered in the chromatographic screening of 40,454 neonates by Giovannini et al [9], whose organization and methods were almost identical with our ones.

In the roughly 70,000 babies of our study, 5 non-PKU cases were found. Three of them were cystinurias detected in the first two years of our programme, when urine specimens were also analysed. These would have been overlooked later when only blood spots were examined. The only patient with histidinaemia needed no therapy, the early diagnosis caused rather unnecessary anxiety in his family. The girl infant with hyperglycinaemia was a seriously ill neonate with vomiting and metabolic acidosis. On the basis of her grave symptoms this child would certainly have undergone more detailed examinations, and her disease could have been diagnosed even without chromatographic screening. All the 6 cases of classical PKU were also discovered by the centralized screening service; the diagnosis made a few days earlier in our local laboratory did not mean a significant advantage in treatment and prognosis.

Our results are in agreement with the well-established international recommendations according to which the only enzymopathies screened for on a population-wide basis should be congenital hypothyroidism, hyperphenylalaninaemia, galactosaemia, and maple syrup urine disease [3, 4, 5, 8, 10]. Since the screening of the first three conditions has been solved on a nation-wide basis in Hungary, and maple syrup urine disease seems to be as rare as about 1 : 150,000 to 1 : 200,000 [2, 4, 12], we have stopped our regional chromatographic screening programme on April 30, 1984.

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