Phenylketonuria: A Reassessment of Mass Infant Screening by Napkin Test*

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Most local health authorities in Great Britain have used the Phenistix test on wet napkins or diapers (napkin-Phenistix test) to screen all young infants for phenylketonuria (Centerwall *et al.*, 1963). This test is a sensitive and reliable method of detecting phenylpyruvic aciduria (Gibbs and Woolf, 1959; Woolf, 1963), which is an early sign of true phenylketonuria (Allen *et al.*, 1964; Berry and Wright, 1967). Some practical difficulties have been emphasized by Hudson and Ireland (1959), but information is lacking on the effectiveness of the napkin test in mass detection programmes. In the Birmingham screening survey (Boyd, 1961) one case was found out of 18,981 tested, which was thought to be adequate, assuming a regional incidence of one in 20,000 births. In Edinburgh a similar incidence was predicted, but the one expected case was missed (Farquhar *et al.*, 1962).

Present Study

With the assistance of the seven local health authorities involved we have investigated 15 true phenylketonurics

TABLE I.—Phenylketonurics Born into Napkin-Phenistix Screening Programmes

Phenistix Result	No. of Patients
Positive { Under 3 months old ..	4 (youngest aged 53 days)
{ Over 3 months old ..	2 (1 aged 9 months; I.Q. 47)
Negative	6 (2 tested under 3 weeks only: 1 in hospital aged 6 weeks)
Not tested	3 (1 ?negative aged 42 days: no record made. 1 only at home aged 5–11 weeks)
Total	15

TABLE II.—Results of 16 Napkin-Phenistix Tests on 12 Phenylketonurics, Related to Age of Testing

Age (weeks)	No. of Tests	Results	
		Positive	Negative
1–3	6	—	6
5–10	4	1	3
> 10	6	5	1

(Stephenson and McBean, 1967) who were born when screening programmes were in operation, between 1960 and 1965. Siblings of previously known phenylketonurics have been excluded from the study. The dates and results of napkin tests were determined from the Child Welfare record cards. The details are given in Table I.

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It is apparent from Table II that all napkin-Phenistix tests in the first three weeks of life were negative, but much more serious is the fact that even in the age group 5–10 weeks only one of four tests was positive.

When the four patients with negative napkin-Phenistix tests over the age of 5 weeks were finally diagnosed they were all obviously affected, and in each case the urine reacted strongly with ferric chloride. Table III shows the serum phenylalanine levels and I.Q. at the time of diagnosis.

TABLE III.—Missed Phenylketonurics: Finding on Diagnosis

Age at Negative Napkin Test	Age at Diagnosis (months)	Serum Phenylalanine (mg./100 ml.)*	I.Q.
5 weeks 2 days	9	26	43 (Cattell)
7 " 1 day	3	70	51 (Griffiths)
9 " 3 days	25	42	46 "
6 months	24	51	50 "

* La Du and Michael (1960).

Conclusions

This investigation shows that the napkin-Phenistix test in a mass screening programme is not an efficient tool for the early detection of classical phenylketonuria. Even the detection rate of 27% under the age of 3 months is probably optimistic, because cases missed towards the end of the period—for example, 1965—may not yet be obviously retarded, and most of the children at risk have not entered school.

A great deal of enthusiasm, hard work, and organizational skill have gone into the execution of these mass screening programmes, but the time has come for such energies to be directed towards more efficient methods of detection.

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