The authors of this paper present a rapid screening test for the detection of phenylketonuria, a metabolic anomaly associated with mental deficiency. This simple method can be used for surveys of large populations.

A NEW SIMPLE TEST PAPER FOR MASS DETECTION OF PHENYLKETONURIA

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SINCE PHENYLKETONURIA, a metabolic anomaly associated with mental retardation, can now often be beneficially treated with a phenylalanine-free diet, it has become desirable to detect its presence as early as possible, since the diet loses its efficacy as the child grows older. At the suggestion of one of us (J.W.) both the Lilly Research Laboratories of Indianapolis, Ind., and later the Ames Company, Inc., of Elkhart, Ind., developed test papers for the detection of phenylketonuria. These small strips of prepared paper may be used by immersion in a fresh urine specimen or by simple pressure against a wet diaper. The Lilly test paper* was released as RT 974 for clinical trial purposes only. The Ames reagent strips are being marketed under the name of Phenistix. The work reported in this paper was done with the Lilly material, but the Phenistix are almost identical in application. With the Lilly test paper the presence of phenylpyruvic acid in the urine produces a color change from the original yellowish white to a blue of varying density, depending on the amount of phenylpyruvic acid present. Amounts as small as 15-20 mg per 100 cc of urine are detectable by this method. The test is not, however, specific for phenylketone; the following substances may also induce color changes as follows: phenol, blue; pyruvic acid, red; paraaminobenzoic acid, red; salicylic acid, purple; hemogentisic acid (alkaptonuria), purple changing to brown. The formation of any color does indicate the presence of some abnormal metabolic product in the urine. With the Ames Phenistix the color change in the presence of phenylketonuria is green, but its sensitivity is otherwise similar. In all positive or doubtful cases, a regular ferric chloride or other confirmatory test on a fresh urine sample is done in our laboratory. False-positives may be found in children taking aspirin or Thorazine.

The test paper was distributed by mail, or handed directly to parents in our clinic, to a total of 1,600 families of retarded children. Six hundred of these cases had been treated in our clinic and 1,000 additional cases were contacted through the mailing lists of the New York Association for the Help of Retarded Children. The test paper was accompanied by a letter and a return postcard, both of which we reproduce herewith:

Dear Parent:

The Association for the Help of Retarded Children is assisting us in discovering cases of phenylketonuria, a form of mental deficiency. This kind of mental deficiency can now be treated successfully. This disease, however, is rare and can be found in less than one out of every hundred mentally retarded children. Early cases respond best to treatment. You can help us find children with this form of mental deficiency by means of a simple urine

* Made by Dr. J. P. Comer of the Lilly Research Foundation.

test which you can do yourself. But this paper test is only the first step in finding out if the child has the disease.

Dip the attached piece of paper into a small amount of fresh urine from your child, and see if the paper turns blue. It may take a minute for the color to change. It will fade away again in a few minutes.

Note the results on the enclosed postcard and return to us to complete your child's record. If you report "no change" or if the paper turns white, then your child does not have this particular disease and you will not hear further from us. If you report a color change or "doubtful," you will hear from us.

Sincerely yours,

Morris J. Solomon Clinic for the Rehabilitation of Retarded Children

NOTE: You can get a urine sample by catching the child's urine in a dish or bottle, or the urine can be squeezed out of a wet diaper. You can also place the paper inside the diaper until the child wets it himself, or you can press it against the wet diaper.

PHENYLPYRUVIC ACID TEST

Date .....

Child's Name .....

Age .....

Address .....

Result of paper test No change .....

Turned blue .....

Doubtful .....

Signed .....
(Parent)

In the first group of 600 cases known to our clinic, 440 postcards (73 per cent) were returned to us, with 12 doubtful results (2.72 per cent of 440), 428 negative results (97.3 per cent of 440) and two positive (0.45 per cent of 440). These two positive cases, of children aged six and seven, respectively, had already been diagnosed. The positive returns, however, confirmed the value of the testing paper as a screening procedure. The 12 doubtful cases proved to be erroneous interpretations by the parents, but in all these instances the urine was again checked in our own laboratory with negative results.

A second group of 1,000 families from the membership lists of the Association for the Help of Retarded Children produced 130 replies (13 per cent) with 130 negative results. Upon telephone inquiry to a random sample of 64 families from this group who failed to answer, we found that in four instances the parents could not be located, 10 families failed to answer for no good reason or because they claimed to have lost the slip, while 26 cases had already been known to the clinic and had already responded to our first survey. In all the remaining cases the patients had already been institutionalized (16 cases) or were so old (eight cases) that the parents thought the test would have no practical meaning for them. It would thus appear that this method of screening provided fairly complete coverage for the cases most likely to be helped.

The chief advantage of this screening device is that it can be carried out by technically untrained people at very little cost. We would therefore recommend that the test be widely used for similar surveys of large populations of retarded children, and that it be adapted by pediatricians as a routine test for infants at least one month of age, since the phenylketonuria may not be detectable during the first weeks of life. The widespread use of the test would furthermore help to support the view that mental deficiency may sometimes represent a treatable disease.

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