Survey of Departments of Health About PKU Screening Programs

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PHENYLKETONURIA (PKU) results from a rare but well-described inborn error of metabolism, usually associated with mental retardation in the untreated state. This hereditary condition is unique among the diseases that may result in mental deficiency: it is readily detected and when diagnosed early in life many authorities report that the deficiency can be modified or prevented by dietary treatment *(1–5)*. Other authorities, however, have questioned the therapeutic value of dietary measures *(6–10)*. They claim that the benefit of the diet is based upon psychological tests that are often inadequate for the measurement of intellectual growth in the newborn. These studies also ignore the inherent bias in an uncontrolled study and the beneficial effect of the additional care and training given a child suspected of having PKU is not taken into account.

Impetus for Study

In the 1950's, the incidence of phenylketonuria was estimated to be only 1 in 40,000 *(11)*, but recent studies and new detection methods have shown a higher rate, ranging from 1 in 10,000 in a 1964 study *(12)* to 1 in 15,000 (reported by Rudolf P. Hormuth, specialist in services for mentally retarded children, Children's Bureau, Department of Health, Education, and Welfare, in a personal communication to Smith in March 1969). Because of the rarity of this disease, many health officials have expressed the belief that monies should be invested in overcoming other health problems whose conquest promises a greater return. Thousands of infants must be tested before one case of phenylketonuria is detected. Thus, to better define the economic parameters of PKU screening programs, we decided to survey selected city health departments and all State and territorial health departments of the United States about various aspects of their PKU programs, such as problems encountered and costs. Under a cover letter, a questionnaire was therefore mailed to 55 health departments; the letter explained the purpose of the survey and requested the departments' cooperation in completing and returning the questionnaire.

Results of Study

Of the 55 questionnaires mailed, 44 (80 percent) were returned; 42 of the health departments reported having a PKU detection program. The survey of the departments of health gave a good indication of how programs differed. The annual cost for an individual program ranged from $4,010 in New Mexico

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Results of survey of 44 departments of health about PKU screening programs

Items reported	Reporting departments	
	Number	Percent[1]
Departments with a PKU program	42	95.5
Departments without a PKU program	2	4.5
Total cost of PKU program:		
Under $10,000	6	13.6
$10,000 to $20,000	10	22.7
$20,000 to $40,000	12	27.3
$40,000 to $60,000	3	6.8
$60,000 to $80,000	2	4.5
$80,000 to $100,000	3	6.8
Over $100,000	2	4.5
Department did not answer question	6	13.6
False-positives detected:		
None	2	4.5
Under ½ percent	14	31.8
½ to 1 percent	5	11.4
1 to 3 percent	8	18.2
3 to 5 percent	0	.0
Over 5 percent	4	9.1
Department did not answer question	11	25.0
Screening test used:		
Guthrie inhibition	38	86.3
Modified Guthrie inhibition	1	2.3
Urine	0	.0
Fluorimetric	1	2.3
Department did not answer question	4	9.1

Results of survey of 44 departments of health about PKU screening programs—continued

Items reported	Reporting departments	
	Number	Percent[1]
Cost per initial screening test:		
Under $0.50	13	29.6
$0.50 to $1.00	17	38.6
$1.00 to $1.50	6	13.6
Over $1.50	3	6.8
Department did not answer question	5	11.4
Confirmatory test used:		
(A) Fluorimetric	12	27.3
(B) LaDu spectrophotometric	2	4.5
(C) Paper chromatrography	2	4.5
Combination of (A) and (B)	2	4.5
Combination of (A) and (C)	13	29.6
Combination of (B) and (C)	1	2.3
Department did not answer question	12	27.3
Cost per confirmatory test:		
Under $1	6	13.6
$1 to $2	6	13.6
$2 to $3	10	22.7
$10	4	9.1
$20	1	2.3
Department did not answer question	17	38.6
Time of administration of initial screening test:		
Under 4 days of age	27	61.3
4 to 7 days of age	13	29.6
1 month of age	1	2.3
Department did not answer question	3	6.8
Time of administration of retest:		
1st visit to physician (6 weeks of age)	21	47.7
6 weeks to 6 months of age	5	11.4
6 months to 1 year of age	0	.0
Never	7	15.9
Department did not answer question	11	25.0
Period on low phenylalanine diet:		
2 to 3 years	2	4.5
3 to 7 years	16	36.4
Up to adolescence	1	2.3
Determined by physician in individual cases	18	40.9
Department did not answer question	7	15.9
Opinions of PKU program:		
Effective	38	86.3
Ineffective	1	2.3
Department did not answer question	5	11.4
Opinions about effectiveness of low phenylalanine diet:		
25 percent effective	0	.0
25 to 50 percent effective	0	.0
50 to 75 percent effective	11	25.0
75 to 100 percent effective	18	40.9
Ineffective	1	2.3
Department did not answer question	14	31.8

[1] Percentages are based on the 44 health departments that responded. Because of rounding, the sum of the percentages for an individual item may not add to 100.0.

to $400,000 in Illinois and California. These differences reflect primarily population variation among the States. In 31 health departments the entire program cost $60,000 or less per year. The two States which had just initiated screening projects reported their anticipated program costs.

The Guthrie inhibition test *(13)* or a modification *(14)* was the primary screening procedure used in 39 programs. Forty health departments reported that the initial screening test was performed within the first week after birth. Twenty-one departments suggested a retest also of the infant at 6 weeks of age. Seven other health departments stated that they did not require retesting but encouraged the patient's physician to retest the infant at the age of 6 weeks. The reported PKU incidence ranged from 1 in 7,500 in Utah to 1 in 24,000 in Illinois; the median incidence rate was 1 in 12,750. The composite mean incidence of the reporting health departments was 1 in 13,796, which corresponds closely with the 1 in 15,000 reported by Hormuth to Smith.

Different health departments used different criteria for a positive PKU diagnosis. The majority, however, used the following criteria: *(a)* two positive screening tests, *(b)* one confirmation test for a serum phenylalanine level of between 18 and 20 mg per 100 ml, and *(c)* a serum tyrosine level of less than 5 mg per 100 ml.

Sixteen respondents stated that a PKU patient usually is maintained on a low phenylalanine diet for an average of 3 to 7 years. Most departments reported 7 years of maintenance of the special low phenylalanine diet. Eighteen departments reported that the length of observance of the special diet was determined by the physician in each individual case.

Forty-one percent of the respondents indicated that the low phenylalanine diet was 75 to 100 percent effective; another 25 percent indicated it was 50 to 75 percent effective; 32 percent did not answer this question; and only 2 percent indicated that the special

diet was ineffective. An overwhelming majority (85 percent) considered the PKU screening program to be efficacious.

Based on the 42 responding health departments that had a PKU program, the numbers of infants screened and the costs were computed. The median number of infants screened per program was 39,374, the median cost of the programs was $25,000, and the median cost per infant was 69 cents. The mean cost per test used was 85 cents, with a range from $0.25 to $5.

The range in costs reflects the number of PKU tests performed, which in turn, reflects both population variations and the length of time the programs had been in effect. The confirmatory test most frequently used was the fluorimetric or a combination of the fluorimeteric and paper chromatography. The reported costs of the confirmatory test ranged from $0.75 to $10, with a median cost of $2.15. The reason some of the tests were so expensive was that few confirmatory tests were run at one time. Because the instrument had to be warmed up and standardized each time, the cost per test increased. Detailed results of the survey are tabulated in the table.

Summary and Conclusions

The data supplied by the 42 health departments that responded to the mailed questionnaire provided the basis from which we computed program costs. These data also can be used to anticipate costs and incidence for a State that does not have a PKU program.

As shown in the table, 95.5 percent of the departments of health that returned the questionnaire had a PKU program. The cost of the programs varied for numerous reasons, but primarily because of differences in the number of patients screened and in the type of test used in the initial screening and the quantitative confirmation. Also, some health departments quoted only the cost of the actual tests, neglecting to add administrative costs, which would make their total program costs higher.

The answers on the questionnaires showed that most respondents (86.3 percent) regarded PKU programs to be effective. However, a few departments indicated that more clinical evidence and experience were needed to fully evaluate the overall merits of PKU detection and screening programs.

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SYNOPSIS

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Mailed questionnaires were used to examine the success of PKU (phenylketonuria) screening programs that were operated by departments of health and to examine differences between these programs. Of 55 questionnaires mailed to health departments, 44 were returned and 42 departments reported they had a PKU detection program.

Thirty-eight respondents considered the PKU detection program to be effective, and 31 respondents indicated that the entire program cost $60,000 or less per year.

The answers and comments on the questionnaires showed a generally positive view of the effectiveness of the PKU screening programs. The responses about the value of the treatment program in general were also positive. However, a few departments indicated that more clinical evidence and experience were needed to fully evaluate the overall merits of PKU detection and screening programs.