

Psychosocial Factors in Maternal Phenylketonuria: Prevention of Unplanned Pregnancies

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ABSTRACT

Background. Women with phenylketonuria (PKU) not treated prior to conception can have a pregnancy that results in serious fetal damage. In this report, factors associated with preventing unplanned (and hence late treated) pregnancies are described.

Methods. Subjects included 60 phenylketonuric women and two comparison groups composed of female acquaintances and diabetic women. All were interviewed and administered tests of intelligence, general well-being, knowledge, and personality.

Results. Thirty-five percent of the sexually active women with PKU used contraception only sporadically. The variables that best predicted reported frequency of birth control use were the extent to which women felt social support to use contraception ($r = .64$) along with positive attitudes about birth control ($r = .66$) and knowledge of family planning ($r = .43$). For the comparison groups, a different pattern of variables predicted contraceptive use, with locus of control figuring most prominently for the diabetics ($r = .39$) and social support for birth control being most important for the acquaintances ($r = .46$).

Conclusions. As more girls with PKU enter childbearing ages, there will be an increased need for specific programs that address psychosocial factors in maternal PKU. (*Am J Public Health* 1991;81:299-304)

Introduction

Maternal phenylketonuria (PKU) as a cause of mental retardation and birth defects is a new phenomenon. In the past, most young women with PKU (an inborn error of phenylalanine metabolism) were mentally retarded and few bore children. Now, most such women are mentally normal, having been born since newborn screening was initiated in the 1960s and treated from early infancy with a phenylalanine-restricted diet.¹ In the United States there may be as many as 4,000 women of childbearing age with PKU,² the majority of whom are at risk for pregnancies that can result in abnormal children. For those with the most severe and most common form of PKU, the frequencies of complications in offspring from untreated pregnancies are 92 percent for mental retardation, 73 percent for microcephaly, 12 percent for congenital heart disease, and 40 percent for low birth weight.³ In fact, it is feared that in the next generation, the consequences of maternal PKU could replace the number of individuals with PKU in whom mental retardation has been prevented by newborn screening.^{4,5}

Dietary treatment will protect the fetus but only under the proper circumstances. Treatment begun prior to conception and continuing throughout pregnancy appears to offer maximum protection, whereas treatment even in the first trimester may not prevent some of the adverse effects of maternal PKU.^{6,7} Since many young women with PKU discontinued the special diet during childhood,⁸ the strategy for preventing birth defects from maternal PKU must include careful family planning so that diet can be initiated before conception.

Tracking adolescents and young adult women with PKU so that they can be advised of the high risk to their pregnancies and the possibilities of treatment is difficult, but with much effort can be done.² In Quebec, there is a registry that tracks individuals with PKU through adulthood.⁹ The results of other tracking efforts, however, indicate that women with PKU usually seek treatment after they are pregnant rather than before.^{7,10,11} The reasons for this are unknown.

The overall purpose of our study is to identify these reasons. We will describe how women with PKU face questions of sexuality and childbearing in order to determine the factors related to preventing unplanned pregnancies in maternal PKU.

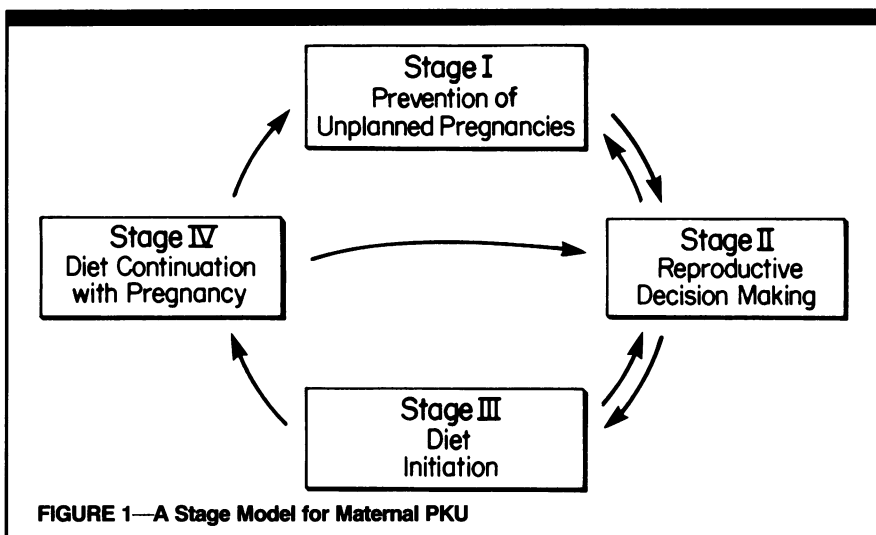
We describe here the findings from the initial interviews of all subjects who were not planning a pregnancy and were not pregnant when the study began in 1985.

Methods

Subjects

Young women in New England known to have hyperphenylalaninemia, ages 16 to 35 years, were invited to participate in a five-year longitudinal study.

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Women with moderate or severe mental retardation were excluded from the sample. Recruiting from clinic lists, newborn screening records, and public health registries, we contacted all women with PKU who met the inclusion criteria regarding age and intellectual functioning. We developed two comparison groups—one consisting of age-matched female acquaintances recruited among those whose names were supplied by the subjects and the other consisting of young women with diabetes, who share childbearing risks and the need for medical intervention prior to and during pregnancy with PKU women.^{12,13} Each diabetic woman, who had been diagnosed for at least one year and had no major medical complications, was individually matched to a PKU subject for age, and whenever possible, for level of education and marital status.

Two hundred and sixty-two women satisfied the criteria for inclusion in the longitudinal study, and 205 agreed to participate. These included 94 percent of the eligible women with PKU, 74 percent of the acquaintances, and 62 percent of eligible diabetics. Among the 205 who participated, 186 were sexually inactive or sexually active but not desiring pregnancy and were enrolled in the phase of the study concerned with preventing pregnancy. These 186 consisted of 60 with PKU, 65 acquaintances, and 61 with diabetes.

Among the 60 subjects with PKU, 53 have the more severe biochemical defects (classic or atypical PKU) that will require resumption of treatment prior to pregnancy.³ Seven of the subjects have mild hyperphenylalaninemia, a less severe biochemical defect often left untreated during childhood. Because it is unclear whether mild hyperphenylalaninemia requires di-

etary treatment during pregnancy,^{14,15} these women were included in the PKU group.

Most subjects with PKU had received a written brochure about maternal PKU and had been invited to maternal PKU education groups. Thirty-eight women had attended at least one group. However, the majority had not attended a PKU clinic within the year prior to the study. As a rule, the women had been advised to plan their pregnancies, begin diet, and reduce blood phenylalanine levels before discontinuing contraception. A few had been advised not to have children and to plan on adoption or to wait until more was known about maternal PKU.

Fifty-eight of the 61 women with diabetes (95 percent) are insulin dependent (Type I), while the other three have been treated only with diet (Type II).

Variables and Procedures

Variables for this study were derived from a psychosocial model we developed to describe the challenges faced by women with PKU during various stages in the maternal PKU life-cycle¹⁶ (see figure 1). These variables were selected from a variety of theoretical approaches and covered background issues, personality, knowledge, attitudes and beliefs, and social support. We chose our initial battery after first developing a list of hypotheses regarding prevention of unplanned pregnancy in maternal PKU. This initial battery was piloted extensively among teenagers and women with no known medical conditions, women with diabetes, and older women with PKU.

The dependent (outcome) variables for those women who reported having had sexual intercourse (the sexually active

group) were frequency of birth-control use, extent of social activities, and a general quality-of-life score. Frequency of birth-control use refers to the regularity with which a woman reported using any contraceptive method. She indicated this by selecting the frequency of use, on a one to seven scale, ranging from "never" to "all the time." The type of birth control method was related to frequency, with oral contraceptives generally being used "all the time" and all other methods being used less often. Hence, for data analysis purposes, the "frequency" rather than "type" of birth control was selected.

The second outcome variable, extent of social activities, measures the types of activities the woman listed that involve social interactions, such as membership in clubs, participation in religious groups, sports, dating, and parties. This variable was selected to determine if women with PKU avoided certain social situations, perhaps due to anxiety about maternal PKU.

The third outcome variable, the General Health Rating Index (GHRI),¹⁷ measures the degree to which people worry about their health, experience pain, or alter their life-style for health reasons. These topics were also explored in open-ended questions. The responses to the open-ended questions were categorized according to whether the answer was neutral, positive, negative, or a combination of these. All ratings were double-scored, and reliability was greater than 95 percent.

For women who reported never having had sexual intercourse (the sexually inactive group), the social activities scores and the GHRI were the outcome measures.

The independent variables included demographic factors, level of intelligence, knowledge about family planning, knowledge about maternal PKU, personality characteristics, social support for family planning, and attitudes and beliefs about contraception, sex, and childbearing.

The interview consisted of introductory questions that provided demographic information. Socioeconomic status was determined using the Hollingshead-Redlich Two Factor Index of Social Position, based on education and job title.¹⁸ Intelligence was measured by the Wechsler Adult Intelligence Scale-Revised (WAIS-R)¹⁹ or the four-subtest short form of the WAIS-R,²⁰ when a full-scale score was not available from clinic records.

A test of fertility and contraception knowledge, adapted from Kempton and Forman²¹ and a test of knowledge about

TABLE 1—Characteristics of the Subjects

	Study Group		Comparison Groups	
	PKU		Diabetes	Acquaintances
Number	60		61	65
Age (mean \pm SD)	20.8 \pm 3.6		21.2 \pm 3.6	20.8 \pm 3.9
Married	7% (4)		12% (7)	11% (7)
Experienced pregnancy	8% (5)		33% (20)	25% (16)
Have child/children	3% (2)		13% (8)	15% (10)
Live with parents	83% (50)		64% (39)	59% (38)
Have driver's license	58% (35)		84% (51)	74% (48)
Education (mean \pm SD)	11.9 \pm 1.7		13.2 \pm 2.1	12.8 \pm 1.8
IQ (mean \pm SD)	86 \pm 14		96 \pm 11	96 \pm 14

TABLE 2—Sexual Activity and Type and Frequency of Birth Control Use among Women with PKU and Comparison Populations

	Study Group		Comparison Groups			
	PKU		Diabetes		Acquaintances	
	%	(n)	%	(n)	%	(n)
Not Sexually Active	57	(34)	29	(18)	34	(22)
Sexually Active	43	(26)	71	(43)	66	(43)
Method of Birth Control						
Oral Contraceptives	46	(12)	32	(14)	51	(22)
Condom	19	(5)	14	(6)	14	(6)
Diaphragm	5	(1)	9	(4)	5	(2)
Sponge	4	(1)	7	(3)	7	(3)
Tubal Ligation	4	(1)	7	(3)	2	(1)
Rhythm	4	(1)	5	(2)	2	(1)
Intrauterine Device	0		0		0	
No method	19	(5)	26	(11)	19	(8)

maternal PKU²² (and a comparable test for women with diabetes) were devised for this study. These tests gave one point for a correct response, with 13 possible points for the contraception knowledge test and ten points for the knowledge of maternal PKU and diabetes tests.

Personality was measured by the Adult Nowicki-Strickland Internal-External Locus of Control Scale²³ and the Rosenberg Self-Esteem Scale.²⁴

Social support for birth control was determined, as suggested by Fishbein²⁵ and Vinokur-Kaplan,²⁶ by asking subjects to name the three people to whom they felt closest and then to rate on a seven-point scale the degree to which each of these people would support their using birth control. The mean ratings constituted the score for social support for birth control.

Attitudes and beliefs were defined by a series of statements to which subjects indicated the extent of their agreement on seven-point scales. These statements, adapted from published studies, were about sexual activity, use of birth control, attitudes regarding contraception, and

past pregnancies.^{27,28} A composite "attitude towards birth control" score was developed from responses to three questions regarding the benefits, advisability, and comfort in using and procuring contraception.

Each woman in the study was interviewed either in her home or at the hospital. All written questionnaires required no more than a sixth-grade reading level. To increase the comfort of the subjects (and to ensure confidentiality), response cards for personal questions concerning sexual activity, birth control, and pregnancy were provided. Each session lasted about two hours.

Data collection also included review of medical records for information on diagnosis and treatment of PKU or diabetes.

Data were analyzed utilizing the Statistical Package for the Social Sciences (SPSS).²⁹ To determine differences between the study groups, chi-square or one-way analyses of variance (with Scheffé tests for pairwise comparisons) were used. Pearson correlations were

used to identify variables related to successful achievement of outcome goals.

Consent procedures standardized by the Children's Hospital (Boston) Committee on Clinical Investigations were followed.

Results

Characteristics of the Sample

Demographic and other background characteristics of the three groups are listed in Table 1. The groups are similar in age, with a mean of approximately 21 years at the time of the study. The frequencies of those who had been pregnant or had a child were less among the women with PKU. Women with PKU were more likely to live with their parents, were less likely to have a driver's license, had fewer years of education, and had a lower mean IQ. Six women with PKU and one acquaintance (but none with diabetes) performed in the range of mild mental retardation, with scores between 60 and 67.

Prevention of Unplanned Pregnancies

As noted in Table 2, 43 percent of the women in the PKU group reported that they were currently or had been sexually active, a smaller proportion than those in the other groups. Among PKU women who had had sexual relations, 19 percent never used birth control, and 65 percent reported always using birth control when they had sexual relations. These findings, along with the type of contraception selected, were similar to those of the comparison groups. As noted in Table 3, married women with PKU were more likely to always use birth control, while unmarried women were less consistent in this respect.

Women with PKU who reported never having had sexual intercourse and those who were sexually active were similar in age, with mean ages of 20.6 and 20.9 years respectively. Less than 13 percent of both groups indicated disapproval of premarital sex and birth control.

The seven women with mild hyperphenylalaninemia did not differ from other women with PKU in terms of the demographic or psychological variables studied, except that they had a more internal locus of control ($F = 9.3$, $SE = .39$). All but two lived with their parents. Their ages ranged from 16 to 22, and their IQ ranged from 78 to 117. Five had had sexual intercourse, among whom two relied on

TABLE 3—Frequency of Birth Control Use among Sexually Active Women according to Marital Status

Use of Birth Control	Comparison Groups		
	Study Group PKU	Diabetes	Acquaintances
Unmarried Women	22	36	36
Never Uses	5	9	6
Always Uses	13	25	27
Married Women	4	7	7
Never Uses	0	2	2
Always Uses	4	3	5

TABLE 4—Pearson Correlations between Independent Variables and Reported Frequency of Contraceptive Use among Sexually Active Women

Independent Variable	Comparison Groups		
	Study Group PKU	Diabetes	Acquaintances
Social Support for Birth Control	.64***	.25	.46**
Attitudes about Birth Control	.66***	.22	.16
Knowledge of Family Planning	.43*	.16	.15
Knowledge of Maternal PKU/Diabetes	.03	.17	—
Personality: Locus of Control	-.14	-.39**	.07
Personality: Self-Esteem	-.08	-.17	.08
IQ	.16	.01	.03
Social Class	0	-.12	-.13

NOTE: Results were similar when analyses were redone controlling for age.
 *p < .05
 **p < .01
 ***p < .001

TABLE 5—Quality of Life among Sexually Active vs. Inactive Women with PKU

	Sexually Active	Sexually Inactive
General Health Ratings Index (mean ± SD)	82.4 ± 16.5	82.6 ± 15.2
Percent women engaged in spare-time activities		
athletics	34.6	38.2
social activities	57.7	82.4
intellectual pursuits	19.2	23.5
solitary	84.6	79.4
Percent reporting alterations in social life due to PKU	19.2	8.8
Percent reporting alterations in plans for future due to PKU	57.7	58.8
Percent reporting alterations in plans to have children	42.3	55.9

the use of condoms intermittently and three used oral contraception.

Factors Associated with Prevention of Unplanned Pregnancy

As noted in Table 4, the degree of social support for birth control that PKU women received from individuals in their social network and their own attitudes about birth control, including comfort in discussing birth control with a health care

provider, were critical factors for contraceptive behavior, correlating .64 and .66 respectively with frequency of contraceptive use. In addition, knowledge of family planning, but not knowledge of maternal PKU, correlated with frequency of contraceptive use. Among women with PKU, personality variables, age, marital status, living situation, IQ, and social class were unrelated to contraceptive use. Multiple regression analyses indicated that when

the variable for either social support for birth control or the attitudes about birth control was entered first in the equation, no other variables were significant.

A different pattern of variables predicted contraceptive use for the comparison groups, with only locus of control figuring prominently for the diabetics and only social support for birth control being important for the acquaintances.

Compared with their acquaintances and women with diabetes, women with PKU attained lower scores on the Knowledge of Family Planning Test (F = 7.8 SE = .14) and had a more external locus of control (F = 9.3 SE = .4).

Quality of Life

As noted in Table 5, for women with PKU, the scores on the GHRI were comparable for those who were sexually active and those who were not. In general, they were involved in similar types of spare-time pursuits, although the women who reported never having had sexual relations were somewhat more likely to engage in social activities. Few of the sexually active or sexually inactive women reported alterations in their social lives because of PKU. Women with PKU who identified negative effects from their disease reported having fewer friends, fewer activities, difficulties explaining their disease to boyfriends, and concerns about becoming sexually involved. More than half in each group reported alterations in their plans for the future due to PKU. Somewhat more of the sexually inactive women mentioned concerns about maternal PKU, and equal numbers mentioned reduced career opportunities as a consequence of PKU-related learning disabilities. Nonetheless, compared with women with diabetes, women with PKU attained significantly higher scores on the GHRI (F = 16.5 SE = 1.5), indicating less worry, less pain, and less of a negative impact from their disease. Fifty percent of women with PKU, compared with 85 percent of women with diabetes, reported undesirable alterations in their social activities and plans for the future as a consequence of their disease.

Discussion

Until now studies of individuals with PKU have focused on intellectual and academic development. However, the necessity for treatment prior to pregnancy in maternal PKU stimulated us to investigate other aspects of development. In this study, we concentrated on those psycho-

social factors in young women with PKU that we believe will be important in their meeting the challenges of family planning in maternal PKU.

We found that many young women with PKU tend to live with their parents and to be without a driver's license. Nonetheless, they are engaged in social activities and competitive employment. They plan to marry and bear children. It is unclear why fewer women with PKU reported having had sexual intercourse compared with their acquaintances and the diabetic women, who were similar in age and marital status. We believe, however, that over the next few years, more will become sexually active. Unfortunately, those who are sexually active seem to be at high risk for unplanned pregnancies, since 35 percent of them report only intermittent use of birth control.

It appears that social support for birth control and positive attitudes about contraception each have a very significant influence on the reported contraceptive behavior of young women with PKU. These findings are consistent with Fishbein's theory of reasoned action, which states that attitudes, social norms, and the willingness to comply with these norms are predictors of behavior.³⁰⁻³²

With the exception of social support, those factors that correlate with birth control use in women with PKU are specific to them and unlike correlating factors in the two comparison groups studied. For instance, their external locus of control does not predict contraceptive frequency; yet in the diabetic subjects and in published studies, an external locus of control is associated with infrequent contraceptive use.^{33,34} On the other hand, knowledge of family planning is significantly correlated with reported frequency of birth control use only in the PKU women. Their knowledge of family planning, in general, is lower than that of the other subjects studied and, in many instances, may be sufficiently low to impair their ability to choose and use contraceptive measures. Education programs such as those described by Cohen and his colleagues in Israel³⁵ may be beneficial to these women. In developing our test of knowledge of maternal PKU, we found that knowledge scores were higher among the 38 women who had attended a PKU education group than among the 22 who had not done so.²² Finally, although the women with PKU have attitudes about birth control that are comparable to those of their acquaintances and the diabetic women, their contraceptive behavior appears to be more

highly influenced by their attitudes. Further analyses show that although IQ is significantly related to knowledge of family planning and knowledge of maternal PKU, it is not significantly related to the frequency of contraceptive use.

In addition to these findings, we gained a keener sense of how women with PKU approach the question of childbearing. The vast majority consider having children a natural sequel to finding a husband, and few acknowledge that an unplanned pregnancy might occur. In these attitudes, they are similar to adolescents confronting a variety of medical and health issues.³⁶

We also learned more about the ways in which women with PKU related to health care providers. As a group, they were extraordinarily cooperative, perhaps reflecting a sense of trust developed over years of association with the PKU programs. Ninety-four percent of those contacted participated in the study. Despite this cooperation, only a few of the women made follow-up clinic appointments. This may be due to apprehension about the blood test and physical examination, to a belief that they already know enough about maternal PKU, or to a presumption that an unplanned pregnancy was not likely to occur.

Women with PKU were self-accepting, as indicated by their responses to the self-esteem questionnaire. Many expressed the thought that they "used to have" PKU when they were children on the special diet. For them, prevention of unplanned pregnancies may have been no different than it was for other teenagers and young adults striving for a sense of identity and independence. The risks to the fetus could easily be forgotten or ignored during this time of self-exploration. This may explain why birth control practices among those with PKU were no better than those of the acquaintances who did not face known childbearing risks. On the other hand, fewer women with PKU were sexually active, perhaps due to fears of unplanned pregnancies, to concerns regarding risks to the fetus, or to limited social opportunities. These speculations regarding the psychological impact of PKU will be explored further as the study continues. Social support will also receive more intensive examination in the continuing study. We plan to define social support more precisely in terms of the nature of support networks, the importance of peers versus family, the role of perceived as opposed to actual support provided, and the extent to which the concept

reflects general support as compared with specific encouragement for birth control use.

As in any study dependent on self-report, the reliability and validity of the subjects' responses should be checked. We asked several duplicate questions, worded slightly differently, so that inconsistent answers about sexual activity and birth control use could be verified. Our sense was that the women were generally honest. Since this is a longitudinal study, each subject will be interviewed at least five times, and further checks can be made on the consistency and reliability of the results.

In the near future as more girls with PKU enter childbearing ages, the need for specific programs for maternal PKU, already serious, will dramatically increase. A critical first step is to develop a registry in the United States similar to that in Canada to track women with PKU so that information and services can be provided. Our society and its health care system must confront the issue of maternal PKU. To ignore the issue is to punish those who because of their inherited condition are at risk for bearing defective children. □

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Conference of Public Health Laboratorians 1991 Kimble Methodology Award

The Kimble Methodology Award, sponsored by the Conference of Public Health Laboratorians and supported by Kimble Glass, Inc., Vineland, New Jersey is intended to recognize significant contributions to the development of diagnostic methodology for use in the public health or diagnostic laboratory. The 1990 Award winners were Dr. Robert E. Weaver and Ms. Dannie G. Hollis, Special Bacteriology Laboratory, Centers for Disease Control, Atlanta, Georgia, for their work on the characterization and identification of numerous genera and species of medically important bacteria.

Nominations are being sought for the 1991 Kimble Methodology Award, (the 40th annual award) to be presented at the annual meeting of the Conference of Public Health Laboratorians scheduled for November 10, 1991 in Atlanta, Georgia. The award consists of a \$1,000 check and a plaque presented by Kimble Glass. In addition, travel and subsistence will be paid for the recipient to attend the 1991 Conference meeting.

The deadline for submission of nominations for the 1991 award is June 17, 1991. All nominations should be entered according to the following rules:

- Nominee's work should be a fundamental contribution, or an adaptation of such, to diagnostic methodology for use in the public health or diagnostic laboratory. Degree of acceptance and use of the methodology will be considered.

- Nominee(s), either an individual or two or more working together, must live and work on the North American continent.

- The nomination (10 copies) shall consist of a letter describing the reason for nomination; the recognition accorded the nominee for the work and the degree of acceptance by and/or its importance to the work of public health or diagnostic laboratories; the curriculum vitae of the nominee; the nominee's current place of employment; a list of the nominee's publications along with reprints of representative recent publications; and, optionally, letters of support for the nomination.

Send nominations to: Hilton T. Goulson, PhD, Kimble Award Chairperson, Department of Parasitology and Laboratory Practice, UNC School of Public Health, CB #7400, Chapel Hill, NC 27599-7400. Tel: (919) 966-3892.