Insurance Coverage of Special Foods Needed in the Treatment of Phenylketonuria

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Synopsis

Optimal medical management of phenylketonuria (PKU) requires the use of special low-phenylalanine foods for many years. For women with PKU, elevated maternal blood levels of phenylalanine even at conception can lead to fetal damage. Despite this need, private health insurance, Medicaid, and other public health programs often exclude the cost of these foods from their benefits.

The New York State Department of Health conducted a survey of metabolic disorders treatment centers to elucidate the problems PKU patients have obtaining and paying for the special foods essential to their care. Payment for special foods was denied to nearly half of those with private health insurance policies and was covered for only 10 percent of Medicaid-eligibles. A public program for children with special health care needs covered these food costs in upstate New York but not in New York City. There is no program of assistance for adults who are not eligible for Medicaid and who do not have private insurance coverage of special foods.

At present, many private health insurance policies and public programs do not cover the costs of low-phenylalanine foods other than infant formula. Payment for this essential part of the management of PKU should be mandated for all public programs for persons with chronic illnesses, public medical assistance (Medicaid) programs, and private health insurance. There is a need for a public program to assist adults with PKU who are not eligible for Medicaid and who do not have health insurance that covers these costs.

THIS REPORT calls attention to the frequent failure of private health insurance, Medicaid, and other public programs to pay for an essential part of the treatment needed by patients with phenylketonuria (PKU) and other inborn errors of metabolism. It is based on information provided by three PKU treatment centers in New York State. Most of the patients of these centers who had health insurance or Medicaid coverage were unable to obtain reimbursement for the costs of the dietary materials needed to control the disorder.

Background

PKU is a relatively common inborn error of metabolism. If untreated or undertreated, it causes severe mental retardation and other serious health problems. It is detectable in the newborn. For the preceding 20 years nearly all infants born in developed countries have been screened for its presence. In New York State alone, 5.9 million infants were screened between 1965 and 1986; 348 cases of classical PKU and 283 cases of hyperphenylalaninemia were identified (*1*).

With proper treatment, mental retardation and most of the other devastating effects of the disorder can be prevented. Treatment consists primarily of restriction of the dietary intake of phenylalanine, an essential amino acid present in most proteins. PKU patients do not metabolize phenylalanine normally, usually because they lack phenylalanine hydroxylase, the enzyme that is responsible for the conversion of phenylalanine to tyrosine. As a result, the concentration of phenylalanine in the blood rises above normal and there is a deficit of tyrosine.

At present, there is no way to replace the absent enzyme. Adequate control of the blood level of

phenylalanine, therefore, can be achieved only through restricting the dietary intake of this amino acid. In essence, this means the exclusion from the diet of almost all protein. Since survival without the essential amino acids is not possible, patients with PKU must obtain their amino acids from a nonnatural source, a manufactured mixture of amino acids that contains at most minute amounts of phenylalanine combined with the other amino acids in the quantities needed for normal growth and development.

Two general types of amino acid mixtures are marketed by pharmaceutical companies. One is designed as a formula for infants. It combines the amino acids with the other components needed for normal growth. The other form is meant to be used by children and adults in conjunction with a diet of the other foods (exclusive of protein) needed for a balanced diet.

If, through the use of these dietary controls, the blood level of phenylalanine can be maintained at or near the levels present in normal persons, most of the harmful effects of PKU can be prevented. This situation is not unique to PKU; similar circumstances are found in other inborn metabolic disorders, such as maple syrup urine disease, homocystinuria, histidinemia, and tyrosinemia. Persons with these conditions also require strict limitation of the dietary intake of a specific amino acid which they cannot metabolize. They have the same need for an alternative source of essential amino acids.

Avoidance of protein-containing foods is relatively easy during infancy but becomes increasingly difficult during childhood and adult life. It means eliminating from the diet protein-containing vegetables and grains as well as milk, eggs, meat, fish, and poultry. Such staples as pasta and baked goods, which are made with wheat flour and milk, must be excluded because they contain significant amounts of phenylalanine. While it is possible to maintain control of blood phenylalanine levels by excluding all of these foods, it is very difficult for a child or adult to tolerate such a restricted diet.

Low-protein substitutes for flour, pasta, baked goods, and gelatin desserts have been developed and marketed. They add significantly to the dietary variety available to persons who are limited to the special amino acid mixtures as their source of protein, and they can make it possible for patients to adhere to the strict diet.

Although the special amino acid preparations are an absolute necessity, and the special low-protein foods are important adjuncts in the treatment of the conditions, many patients with PKU and other metabolic disorders find that their health insurance does not cover the cost of these foods.

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The importance of the special amino acid mixtures is reflected in the policy published by the American Academy of Pediatrics in 1979, "Reimbursement for Medical Foods for Inborn Errors of Amino Acid Metabolism." It states (*2*):

> . . . amino acid modified products used in the treatment of the aminoacidopathies are medical expenses which should be reimbursed, in whole or in part, under major medical and comprehensive group policies and CHAMPUS.

Before 1977, it was generally believed that restriction of dietary phenylalanine was necessary only during the first few years of life, the period of most rapid brain development. Most treatment centers discontinued patients' dietary controls at about 6 years of age, even though there was little evidence that this discontinuation was entirely safe (*3*). Since then, many studies have shown that children whose blood phenylalanine concentrations have been controlled beyond 6 years of age tend to perform better on intelligence tests than children whose blood levels have not been controlled (*4–8*). In 1987, Koch and Wenz reported data from the National Collaborative Study of Children Treated for PKU, which showed that this effect could be demonstrated through at least 12 years of age (*9*).

It now appears that elevated levels of blood phenylalanine may be harmful well beyond 6 years of age. Intelligence testing indicates that scores correlate with the age at which dietary control is lost (*10*). Optimum development may, therefore, require dietary control for a much longer time, perhaps even for the lifetime of the affected person.

For pregnant women, the need to maintain dietary control has additional urgency. Elevated maternal blood phenylalanine levels may damage

Table 1. Cost of low-phenylalanine special formula foods

Product	Package size	Protein equivalent (percent)	Wholesale cost[1]	Cost per gram of protein equivalent
Analog XP[2]	3.5 oz	13	$ 3.60	$0.264
Lefenalac[3]	16 oz	15.1	19.77	0.288
Maxamaid XP[2]	7 oz	25	13.80	0.263
Maxamum XP[2]	7 oz	39	21.60	0.264
Phenyl-Free[3]	16 oz	20	26.49	0.292
PKU 1[3]	500 g	50	77.46	0.310
PKU 2[3]	500 g	67	91.53	0.273
PKU 3[3]	500 g	68	91.53	0.269

[1] Average wholesale price listed in 1992 Drug Topics Red Book, Medical Economics Data, Montvale, NJ, 1992.
[2] Ross Laboratories, Columbus, OH.
[3] Mead-Johnson, 2400 West Lloyd Expressway, Evansville, IN.

the fetus in utero (*11–15*). The mechanism that produces the injury is incompletely understood, but it appears to be related to the deprivation of the developing brain of amino acids needed for normal development. Elevated levels of phenylalanine in the fetal circulation apparently block the transport of other amino acids across the blood-brain barrier (*16*). In addition, elevated maternal phenylalanine concentrations interfere with the normal transit across the placenta of the amino acids tryptophane and tyrosine (*17*).

Fetal damage may occur at the earliest stages of pregnancy (*18*). Dietary treatment started after conception does not protect babies whose mothers' phenylalanine levels are above normal at the time of conception. Only babies whose mothers' phenylalanine levels were at or near normal *at the time of conception* grew optimally.

This new problem is a direct result of the success of the newborn screening program. The detection of PKU in the newborn period and the effective treatment of the condition has produced a new generation of women who, despite having the metabolic defect, have reached childbearing age as normal and healthy adults. However, the continued presence of the metabolic disorder results in an extreme danger to their children, even though the children do not inherit the metabolic defect. If the concentration of phenylalanine in the mother's blood is greater than 10 milligrams per deciliter (0.6 millimoles per liter) at the time of conception, the child is likely to be permanently damaged. Exposure to elevated levels at any time during the course of the pregnancy is also likely to be harmful.

To protect the embryo from damage, a woman who does not metabolize phenylalanine normally must maintain control of her dietary intake of phenylalanine as long as she is at risk of becoming pregnant. This control is possible only through the use of the special amino acid mixtures and the elimination from the diet of other sources of protein, as discussed previously. Of the 4.6 million women in New York State between the ages of 12 and 44, it is estimated that 491 have PKU or hyperphenylalaninemia. Normal development of their children depends on the maintenance of safe maternal blood levels of phenylalanine from the time of conception and throughout pregnancy.

Recognizing "the potential for major birth defects to occur in children whose mothers have phenylketonuria (PKU) . . . and even mild forms of hyperphenylalaninemia . . .," (*19*) the American Public Health Association in 1989 recommended actions to alleviate the problem. It encouraged the passage of legislation

> . . . to require all third party payers, including insurers and federal and state programs . . . to cover the costs of medical foods required for implementation of the phenylalanine-restricted diet for all women at risk throughout their childbearing years.

Patients who have been released from the constraints of the low-phenylalanine diet and allowed to eat all foods find it most difficult, if not impossible, to again accept the restrictions (*20,21*). Attempts to re-start the diet for children and young adults had a high failure rate. Few of those who re-start the diet achieve optimal degrees of control of blood phenylalanine. For this reason, there is increasing support for the policy of keeping female patients on the low-phenylalanine diet until they are no longer at risk of having children. Elevated blood phenylalanine concentrations have also been reported to have adverse effects on males, specifically in decreasing sperm production (*22*). For these reasons, the major treatment center for the population of Ireland, which has a high incidence of PKU, advocates "diet for life" for all patients (*23*).

Elevated blood phenylalanine levels in older patients of both sexes have also been associated with behavior and learning problems which are reversed when the blood levels return to relatively normal levels after resumption of dietary control (*6,24*).

The special medical and low-protein foods used to treat PKU are expensive and can be a significant burden to families. A 1986 study indicated that a pregnant PKU patient spent approximately $370 per month on these products (*25*).

Table 2. Patients with private health insurance and Medicaid coverage of special foods needed to manage phenylketonuria

Location	Patients younger than 21			Patients 21 and older			All patients		
	Private	Medicaid	Total	Private	Medicaid	Total	Private	Medicaid	Total
Center 1.....	11	7	40	2	2	6	13	9	46
Center 2.....	30	5	35	0	1	1	30	6	36
Center 3.....	61	44	138	13	3	16	74	47	154
Total.....	102	56	213	15	6	23	117	62	236

The cost of the special amino acid mixtures is responsible for most of this burden (table 1). For example, Maxamaid XP, a product marketed by Ross Laboratories and widely used for children with PKU, costs the pharmacist about $13.80 for a 7-ounce container, or 26 cents per gram of protein equivalent amino acid mixture. Maxamum XP (Ross Laboratories), for adults, costs $21.60 for 7 ounces, but since its amino acid content is more concentrated, the cost per gram of protein equivalent is the same. Phenyl-free (Mead-Johnson) costs the pharmacist about $26.49 per 1-pound can, or about 29 cents per gram of protein equivalent. For a child consuming 30 grams per day, the cost (to the pharmacist) therefore is approximately $8.40 per day, or $3,066 per year; for an adult using 45 grams per day, the cost would amount to $4,599 per year.

The cost of special low-protein foods is also relatively high. For example, a 9-ounce can of low-protein white bread costs $3.19; a 6-ounce box of cookies, $2.34; an 8.75-ounce box of macaroni, $3.02; and a 4-pound bag of baking mix, $7.16.

Method

To determine the size and characteristics of this problem, in February 1990 the New York State Department of Health sent questionnaires concerning the use of special foods to the centers for inborn metabolic disorders in the State. Information was gathered about the special foods that the centers prescribed for patients with PKU and other inborn metabolic disorders, how the centers assisted patients to find suppliers of the foods, and how patients paid for the foods. Centers were asked to report the number of patients for whom foods were paid for by private health insurance, Medicaid, and the State program for children with special health care needs (called the Physically Handicapped Children's Program in New York).

Responses were received from centers located at the University of Rochester Medical Center, Robert Warner Rehabilitation Center of Children's Hospital of Buffalo, and Bellevue Hospital Center in New York City. This report summarizes the information that they provided.

'To protect the embryo from damage, a woman who does not metabolize phenylalanine normally must maintain control of her dietary intake of phenylalanine as long as she is at risk of becoming pregnant. This control is possible only through the use of the special amino acid mixtures and the elimination from the diet of other sources of protein, ...'

Results

The centers reported that they currently prescribed special foods other than low-phenylalanine infant formulas for 213 patients younger than 21 years and 23 patients older than 21. The foods included noninfant mixtures of amino acids and low protein foods such as pasta, bread, crackers, cookies, baking mix, and jelled dessert mix.

Half of the patients (117) were covered by private health insurance and one-quarter (62) by Medicaid (table 2). However, most patients found that the formula and foods that they needed were excluded from coverage. This was true for 44 percent of those with private insurance (table 3) and 90 percent of those with Medicaid (table 3). Both Medicaid and private health insurance usually paid for low-phenylalanine infant formula.

Another potential source of support for families in New York State is the Physically Handicapped Children's Program (PHCP), a joint State and county program to assist families to obtain health services for children with special health care needs. Through this program, funds are available to pay for medical services needed for children with

Table 3. Private health insurance and Medicaid coverage of special foods needed to manage phenylketonuria

Source and location	Number of patients	Usually paid for foods prescribed		Usually did not pay for foods prescribed	
		Number	Percent	Number	Percent
Insurance.....	117	66	56	51	44
Center 1....	13	5	38	8	62
Center 2....	30	5	17	25	83
Center 3....	74	56	76	18	24
Medicaid	62	6	10	56	90
Center 1....	9	6	67	3	33
Center 2....	6	0	0	6	100
Center 3....	47	0	0	47	100

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chronic health problems up to the age of 21. The metabolic disorders centers reported that 57 PHCP-eligible children who lived outside of New York City had had special foods paid for by the PHCP, but that 14 eligible children who lived in New York City had not. The New York City program covered the cost of special formula for infants but not the cost of special foods for older children. For persons older than 21 years, New York State has no assistance program comparable to the PHCP.

Discussion

It is understandable that the coverage provided by private health insurance is not uniform, since contract terms vary. However, it is surprising to find that coverage under public programs is also inconsistent. While Medicaid paid for special foods prescribed for six of nine patients cared for at one center, the other two centers reported that payment had been refused for all 53 of their Medicaid-covered patients.

These differences may have been the result of coverage decisions made at the regional office level of the program. It is also known that some initial decisions not to cover special foods were reversed after Medicaid recipients appealed through a fair hearing process. In April 1992, the State Medicaid office modified its policy concerning special foods for PKU patients (personal communication from the Office of Health Systems Management, New York State Department of Health, April 14, 1992). Medicaid patients in all parts of New York can now have the costs of these foods covered.

In New York State, individual counties and the city of New York determine which services will be covered under the PHCP. As a result of this policy, county PHCPs paid for special foods for the 57 children who lived outside of New York City, but the New York City program did not cover the cost of the foods for the 14 children who lived in the city.

The centers reported that many families considered the cost of these special foods to be a major burden. Their staffs interceded for patients by appealing to private insurance carriers and to local Medicaid offices to attempt to reverse decisions which had denied reimbursement for special foods. They reported that their efforts were rarely effective.

Finding a supplier of the special foods rarely caused any difficulty. The specialty centers provided patients with names and addresses of mail order and local suppliers. They reported no difficulty obtaining formula through local pharmacies. Two centers kept on hand samples of all low protein foods prescribed. One dispensed them to families as needed. Foods for this purpose were purchased with funds donated by local community groups. One center stocked and supplied only low-phenylalanine infant formula.

One center reported that it had encouraged and assisted a local pastry shop to bake and market low protein breads, cookies, and cakes. It had also arranged to have a local pharmacy order and deliver special foods for Medicaid patients.

Recommendations

Efforts should be made to ensure that private health insurance and public programs cover these costs. The New York Medicaid Program has recently changed its policy regarding special dietary materials for PKU and now allows reimbursement for them; the State PHCP has encouraged local programs to cover these materials (unpublished report of the New York State Physically Handicapped Children's Program, "Guidelines for special PKU foods for older children: a memorandum to local PHCPs." Albany, August 1988). In addition, legislation has recently been introduced to require health insurance to cover the cost of the special medical foods for PKU (personal communi-

cation from Assemblywoman Elizabeth A. Connelly concerning New York State Assembly Bill 5943. Albany, April 28, 1992).

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