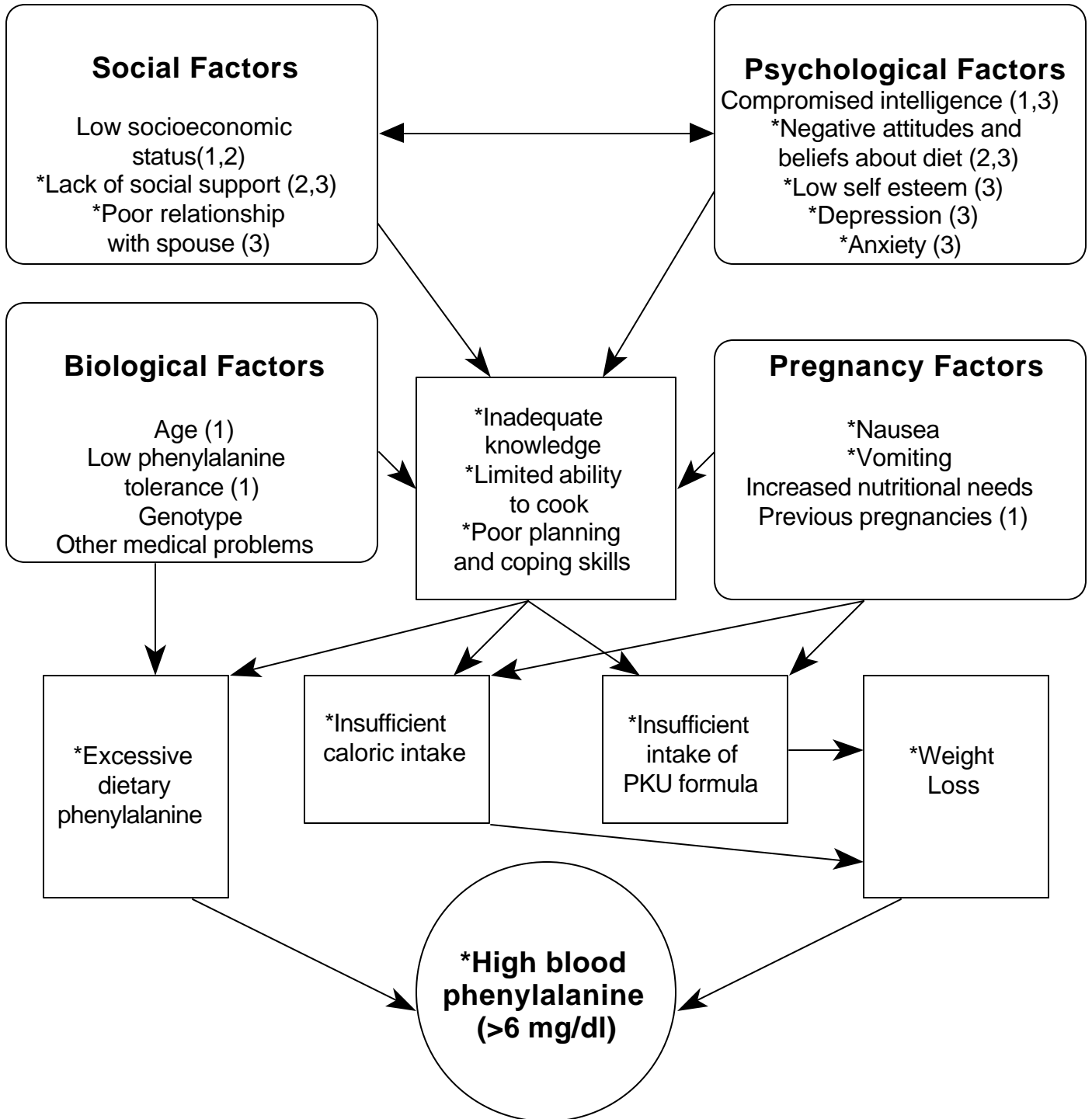


Possible Factors Leading to High Phenylalanine Levels in Maternal PKU



*Factors amenable to psychosocial support and practical assistance with diet

Possible factors leading to high phenylalanine levels in maternal PKU

Explanation of the model

The most important variable in determining the well-being of a child born to a mother with PKU is how quickly the mother achieves metabolic control, i.e. how soon phenylalanine levels get to and remain between the 2-6 mg/dl. Intake of too much phenylalanine, insufficient calories or insufficient formula can all lead to high phenylalanine levels and are indications that the woman is having difficulty managing the diet. The biological, psychological and social reasons for inability to handle the diet are complex and interdependent; some of these are amenable to change and others may be beyond the scope of intervention.

From a nutritional standpoint, there are two conditions which can cause high blood phenylalanine levels: the woman consumes excessive dietary phenylalanine, or she is in a catabolic state. Catabolism is a metabolic state of protein breakdown which is caused when a person has consumed insufficient calories or protein and relies on body stores of protein to meet these needs. In the PKU diet, about 85% of protein is supplied by the PKU formula in a modified form without phenylalanine, therefore insufficient formula intake also leads to catabolism, which if prolonged causes weight loss. Catabolism is also caused by illnesses, particularly febrile, which increase metabolic rate and therefore protein and energy needs. Excess dietary phenylalanine comes from eating more natural protein (i.e. protein containing phenylalanine unlike formula protein). This happens when the woman is not following the diet as recommended, or if the diet that was recommended was incorrect.

How some women can successfully implement a low phenylalanine diet while others can not is an important question to be considered in planning intervention strategies and defining treatment protocols. Through our involvement in the Maternal PKU Collaborative Study, the Study of Psychosocial Factors in Maternal PKU and an independent evaluation of the Resource Mother's program, as well as through our personal experience with nearly 50 maternal PKU pregnancies and reviewing literature on intervention programs, the New England Maternal PKU Planning Group has begun to identify factors that lead to successful adjustment to a maternal PKU pregnancy and positive birth outcomes.

The proposed model includes the social, psychological and biological factors that impact a woman's ability to implement the diet and which research has determined these factors to be predictive. Research on pregnant women in general corroborates the findings that poverty, psychological problems and lack of social support are risk factors for poor pregnancy outcomes. The demands of a PKU pregnancy can put women with marginal psychosocial situations into an "at-risk" category.

Some of the identified factors are beyond the influence of a treatment protocol and belong to cultural, societal or genetic realms that are immutable in the short term. Despite the broader scope of the problem and regardless of the specific risk factors a woman possesses, provision of social support and practical assistance can help women with PKU better cope with their diets and bring phenylalanine levels into a desired treatment range - thereby increasing the chances for a healthy outcome.

Factors causing high phenylalanine levels in Maternal PKU

1. Weight loss

Before pregnancy

Women should be classified as normal, over or underweight based on their prenatal weight and height (Appendix 2 -Part 4 Nutrition Support Protocol).

Women planning pregnancy should never try to lose weight as it can compromise nutrient intake and status at a time when maternal nutrient stores should be replete. In addition, weight loss can cause high phenylalanine levels associated with lean body mass catabolism. A woman who is underweight prior to conception should be encouraged to gain weight before pregnancy. The Maternal PKU Collaborative Study (MPKUUCS) showed that women who were underweight for height before pregnancy were less likely to gain the recommended amount of weight during pregnancy, which had a negative impact on pregnancy outcome.

During pregnancy

Women should be classified as normal, over or underweight based on their prenatal weight and height (Appendix 2 -Part 4 Nutrition Support Protocol). Women with PKU should gain weight normally during pregnancy despite the fact that they follow restricted diets. The optimal amount and pattern of weight gain for each weight category is defined in the nutrition protocol. Weight gain during pregnancy is a predictor of birth outcome in maternal PKU. Next to blood phenylalanine levels, the percent of recommended weight gain during pregnancy was the most important predictor of the infant's birth weight, length and head circumference in the MPKUUCS.

Inadequate weight gain or weight loss during pregnancy

Inadequate weight gain is due to either insufficient protein intake or insufficient caloric intake. Protein and energy intakes are interrelated; adding more calories if the protein intake is low is futile. Insufficient protein intake occurs when the amount of medical food (formula) prescribed is insufficient and/or the woman is having difficulty consuming the proper amount of medical food. Do not easily disregard the possibility that the woman is having difficulty consuming the full amount of medical food if her weight gain is inadequate or her phenylalanine levels are high even if she reports adherence to taking the medical food (see section on formula intake below).

Weight loss will result in high blood phenylalanine levels due to catabolism of lean body mass releasing endogenous phenylalanine and needs to be corrected rapidly.

Unfortunately, in pregnancy weight loss is often due to nausea and vomiting, making it difficult for the woman to get sufficient calories. Formula is often not tolerated which compromises protein, energy and overall nutrient intake. If usual corrective measures for nausea and vomiting are not working, hospitalization for nutritional repletion (including parenteral nutrition in severe cases) is recommended.

2. Insufficient Caloric Intake

Assessing energy intake

Analysis of a 3 day food record or food intake recall is needed to determine energy intake. Energy needs are defined in the nutrition protocol. If the woman is not meeting these

guidelines, add sources of energy to provide sufficient calories. If the woman is meeting these guidelines, getting sufficient medical food and still not gaining weight, she may have a higher caloric requirement due to her activity, stress level or even insomnia. Regardless of the reason, more calories are needed. Given the limitations of the diet, extra calories can be added only from fats, sugar, and low protein specialty products.

Checking fat intakes

Make certain the woman is getting adequate fat (30% of kcal). Women in the MPKUCS tended to have lower than recommended fat intakes. In this age of fat phobia, many women use low fat/non fat salad dressings and other products - these should be avoided. Give a specific number of servings of high fat foods to be eaten each day, rather than general guidelines as her idea of a lot of fat may be quite different from yours. Ideas for increasing fat intake include:

- Fried foods (use soy or canola oil for the best essential fatty acid profile)
 - peppers, mushrooms, onions added to tomato sauce
 - stir fry vegetables over low protein rice
 - vegetable tempura (see Low Protein Cookery)
- Added fats (margarine, Miracle whip, butter, mayo)
- Rich's Rich Whip or Cool Whip (NOT Lite)
- Coffee rich (use on cereals, in soups, shakes, formula)
- Canned frosting (eat right out of the can as a snack)
- Regular salad dressings
- Extra olive oil on salads in addition to dressings
- Vegetable dips (low pro Ranch dressing is a favorite)
- Chocolate or almond bark
- Duobars (Scientific Hospital Supplies)(expensive but worth a try)
- Oil added to the formula (is distasteful to some; others don't mind)

Sucrose

See free foods in the nutrition protocol.

Some women object to eating sugary foods and need to be reassured that some of these foods are included in the diet to provide sufficient calories. Women with gestational diabetes should avoid these foods, however there is no evidence that dietary sucrose ingestion causes gestational diabetes.

Low Protein Specialty Products

Low protein products such as flours, breads, crackers, cookies and pastas offer much needed variety and energy to the MPKU diet. They are made from flour which has had the highest protein containing compartment removed rendering the flour much like a cornstarch consistency. The greater the acceptance and use of these products, the greater the adherence to the diet and weight gain.

It helps to identify a few low protein "staples" such as bread or pasta that can be used as a basis for meals.

Low protein foods are available by mail order in the United States from the following companies:

Dietary Specialties, Rochester, NY
EnerG Foods, Seattle, WA
Med Diet, South Minnetonka, MN

All of these companies offer both ready-made products and flours for making you own bread, cookies, cakes, and snack foods. Recipes using these products are available from the companies or in low protein cookbooks such as Low Protein Cookery for PKU and Bread Machine Baking for PKU (both by Virginia Schuett).

The key to success in using low protein foods is to work with a person who has experience using such products and can help identify simple, satisfying recipes that can be substituted for high protein foods. Too often, women start off the diet eating only fruits and vegetables; after a few weeks the diet becomes monotonous, the woman loses weight (driving up blood phenylalanine levels) and becomes discouraged about the lack of variety in the diet, which increases the likelihood of her not adhering strictly to phenylalanine limitations.

Because of the importance of the specialty low protein foods in maintaining the PKU diet, several states have mandated that insurance cover the cost of such products. In other states, the metabolic centers provide these foods to their patients. If there is no means to pay for the specialty products, private charities should be approached for donations.

3. Insufficient intake of PKU formula

If women do not consume adequate amounts of phenylalanine-free formula during pregnancy, they easily become catabolic (a metabolic state of protein breakdown which causes high phenylalanine levels and weight loss) for several reasons. Due to the accretion of lean body mass and the growth of the fetus, the demand for protein is high in pregnancy. Moreover, when protein is provided as L-amino acids, as it is in formulas, the requirement for protein may be even higher because amino acids are oxidized more rapidly than whole protein. Medical foods usually provide about 85% of a pregnant woman's protein needs. If a woman's phenylalanine levels are high, especially if her weight gain is inadequate, careful assessment of formula intake is needed.

Because of the characteristic taste and odor of the medical foods, they may be especially difficult to tolerate during the early weeks of pregnancy when nausea and vomiting are common. Women are sometimes reluctant to admit having difficulty with formula intake because they are emotionally overwrought knowing that they can not tolerate the formula and fearing the consequences to the infant. Others may not keep close track of the amount of formula they have consumed, and report taking the amount they have been prescribed. Still others may not understand the importance of taking the formula to achieving metabolic control and proper nutrition.

If taking formula is deemed to be the problem, several options exist:

1. Flavor the formula. Flavoring ideas are provided in the Nutrition Support Protocol (Appendix 2-Part 4).

2. Drink formula from a covered cup or sports-type bottle to reduce the odor.
3. Chew gum, have hard candy or brush teeth after taking the formula to reduce the aftertaste.
4. Try a different formula - a comparison of formulas available is provided in the Nutrition Support Protocol (Appendix 2-Part 4) .
5. Take some formula as bars. If this option is chosen, reassess overall vitamin and mineral intake, as the bars provide amino acids, but not vitamins and minerals.
6. Take some formula as capsules. This requires packing the formula into gelatin capsules (available from Frontier Cooperative Herbs, Norway, IA). It is best to use PKU-3 (Mead Johnson, Evansville, IN) because it is the highest in protein and requires the least number of capsules and less packing. A video explaining how to pack and use capsules for maternal PKU may be loaned from Children's Hospital, Boston.

References

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2. St. James PS: The Resource Mothers Program for Maternal PKU: An Ecological Approach to Intervention and Program Evaluation. Dissertation, U Mass, Boston; 1996.
3. Waisbren SE et al: Psychosocial factors in maternal phenylketonuria: Women's adherence to medical recommendations. Am J Pub Health 1995;85:1636-1641.