



Outcomes beyond phenylalanine: An international perspective [☆]

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ABSTRACT

Control of blood phenylalanine (Phe) levels throughout the life of a person diagnosed with phenylketonuria (PKU) is the biochemical management strategy necessary to provide the best potential for optimal outcome. Psychosocial support mechanisms comprise the other aspects of PKU management that are necessary to overcome the hurdles of living with this chronic disease and to adhere to the rigors of its management. Additional psychosocial support may be required, in light of increasing evidence that control of blood Phe levels in PKU can still lead to subtle but measurable cognitive function deficits as well as a predisposition to certain psychiatric symptoms and disorders. An all encompassing PKU management strategy that goes beyond simply treating blood Phe levels can empower and enable people born with PKU to achieve similar life goals as those born without PKU. This review looks at PKU management strategies that go beyond treating Phe levels, specifically (1) the roles psychologists play in managing PKU from infancy through adulthood and how they help PKU families and caregivers deal with the disease and the burden of its management; (2) understanding the challenges of transitioning into adulthood as an individual with PKU and addressing unmet needs in this population; (3) how non-traditional practices can be utilized in PKU. The objective is to emphasize that management of PKU goes well beyond addressing the biochemical nature of this disease in order to achieve optimal patient outcomes.

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Introduction

The interplay between nature and nurture is part of the foundation of human beings. When these two factors are not in harmony, there is a risk of developing disease. Being born with two mutated copies of the phenylalanine hydroxylase (PAH; EC 1.14.16.1)¹ gene is the basis for phenylketonuria (PKU; OMIM 261600 and 261630), resulting in deficient PAH activity and subsequently elevated blood phenylalanine (Phe) levels [1]. Left untreated, elevated blood Phe in PKU can lead to severe mental deficiencies. Medical science has

not yet reached the level of sophistication required to correct nature's mistake, and while replacing deficient PAH genes with functional copies is the "holy grail" of PKU therapy, technological hurdles maintain it out of reality's reach [2]. Instead, control of Phe levels in PKU requires lifelong management using a diet that restricts intake of Phe for most individuals with the condition. Recently, non-dietary therapies became available to supplement the dietary regimen for PKU, and additional innovations in treatment are being investigated.

It is widely appreciated by the medical community that strict control of blood Phe levels in PKU is an absolute requirement to enable individuals with PKU to become functional, contributing members of society with normal intelligence quotient (IQ) and social development. However, what may be underappreciated is the crucial role that psychosocial interventions can play in PKU management to ensure optimal outcomes. Psychosocial support mechanisms can help parents cope at the time of diagnosis. Additionally, psychosocial support can aid parents, caregivers, and individuals with PKU to deal with the rigors of adhering to the strict diet as well as the stressors of living with a chronic medical condition.

Furthermore, there is strong evidence that individuals with PKU who achieve good blood Phe control may still be at higher risk for living with cognitive deficits and psychiatric dysfunction compared to the general population [3]. Therefore, additional psychosocial

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¹ Abbreviations used: PKU, phenylketonuria; Phe, phenylalanine; PAH, phenylalanine hydroxylase; ADHD, attention deficit hyperactivity disorder.

mechanisms are required to identify and treat individuals with PKU who may otherwise be unnecessarily living with the burdens of a disease that is affecting their ability to reach their full potential. This review explores many of the social and psychological facets of PKU management that can be utilized to optimize PKU patient outcomes. This issue will be explored in four perspectives, offering a diverse international voice on psychosocial support mechanisms deemed of particular importance by four authors who are all frontline PKU health care providers in their respective countries.

Integrating psychological information in clinical practice

As stated by Scriver and Lee, “beyond the diagnostic phenotype, whatever its name, there is the patient” [4]. The patient outcome is much more complex than the sole consequences of Phe levels on the brain. PKU will induce many disturbances in the family structure, and diet treatment by itself may have some specific burden to the individual with PKU and their family.

In a recent European survey about the practice of PKU management in more than 160 European centers, 65% of the centers responded indicating that they have a psychologist as part of the team [5]. However, 35% of European centers and the majority of North American centers (Burton, personal communication) are without a psychologist, even though the role of the psychologist is very important to the management of PKU. Therefore, the overall consequences of PKU extend beyond the disease itself. Our objective is to determine the role of the psychologist in the management of individuals with PKU from birth to adulthood.

Diagnosis announcement: from initial shock to reality

The first step in PKU management following neonatal screening is the announcement of diagnosis. This is always a traumatic experience for parents, who have to come to terms with their baby's health challenges ahead. Even after many years, when the child's PKU is well managed and everyone in the family has adjusted to the new lifestyle, parents can still describe the terrible moment when the diagnosis was first announced. This initial shock of diagnosis is heightened since the baby with PKU initially appears to be in good health. The diagnosis may seem like a complete intrusion of the medical world into a family who was otherwise unprepared with no prior signals of a disturbance.

To decrease the impact of trauma, a psychologist or social worker may be introduced during the first interview, when the pediatrician explains the disorder to the parents. Once the pediatrician leaves, that individual can go over all the explanations with the parents and can provide further support for them at this difficult moment. As early as possible, it is desirable to arrange for new families to meet with experienced families who are willing to give evidence of the excellent outcome of their PKU child. This seems to be the most efficient way to decrease the burden of the initial diagnosis.

Addressing psychological problems

During infancy and the early school years

An individual's IQ is strongly related to the quality of metabolic control during infancy, which is why a strict diet is recommended for the first 10 years of life. Nevertheless, even when metabolic control is maintained, some children experience attention deficit hyperactivity disorder (ADHD), which can lead to poor academic performance [6,7]. The onset of ADHD may be due to a modifying gene known as MAO-B, which can trigger the increase of phenylethylamine (a toxic metabolite of Phe) when it is impaired [8].

Moreover, neuropsychological studies have shown that children with PKU face some difficulties in mathematics [9]. PKU children may be at higher risk for these neurocognitive issues and ideally should undergo routine periodic and systematic neuropsychological assessments. As is the case of all students identified with learning disabilities, a psychologist should collaborate with school personnel to develop an appropriate educational plan, with support services and modifications (such as extended testing time or permission to use a calculator) that address the child's specific learning needs.

Failure of PKU treatment may be related to parents' inability to administer a low-Phe diet to their child. Reasons for failure can be attributed to family situations and backgrounds [10] as well as barriers with language, psychological, and cultural communication [11], all of which can affect optimal comprehension of the disorder and what is necessary for treatment. Some parents cannot bring themselves to impose the diet on their child [12]. The success of parents in enforcing adherence to the diet often appears to parallel their general parenting skills. Those parents who are themselves accepting of the diet and view it as non-negotiable with the child typically exhibit the greatest success. The stress of having to administer the diet can be worse on the family than the risk on the child's health. Therefore, family therapy may be one of the most effective interventions when dietary recommendations are not followed. Finally, as with many other chronic conditions (e.g., diabetes), the quality of the follow-up depends on the family's motivation and comprehension of the disorder [13].

During adolescence

The main challenge during the period of adolescence is the typical relaxation of the diet that occurs in this age group, regardless of the guidelines proposed by the medical team. There is an absence of perception of any immediate harm linked with a relaxed diet, and the benefit and pleasure of food becomes more important to the individual. The primary obstacles often cited to better adherence are time constraints and stress associated with food preparation and record-keeping, and the restrictions imposed on social life [14]. These obstacles can be amplified by parental maladjustment to chronic illness [15]. Initiatives to improve child adaptive functioning and parental support as well as practical assistance to help parents meet their child's health needs may reduce parental stress and family disruption in this population.

Many studies have reported psychological disturbances in older children or adolescents with PKU [16–20]. Internalizing problems such as depressive mood, anxiety, physical complaints, or social isolation are significantly more common in individuals with PKU, whereas externalizing problems are not [17,20]. Weglage et al. [17,18] also showed that patients are characterized by less autonomy, more negative evaluation of their scholastic ability, less achievement motivation, low frustration tolerance, more negative self-description, less extroversion and impulsiveness, a feeling of not being quite healthy, and feeling that they are less independent. Individuals with PKU may see their social situation as being distinctly restricted. These psychological attributes have been found equally in patients with diabetes and may be related to the burden of a chronic condition [17].

Psychological assessment is clearly important during adolescence, and it must include an assessment of the cognitive level of the individual as well as the psychological status of the individual and family. Education on the development of autonomy must be proposed as soon as the child is 16 years old and must be adapted to each teenager and to each family. In some centers, the parents are no longer allowed to accompany the child to the PKU clinic. It is important that this transition be made without disrupting the parent-child relationship, which remains essential [21]. PKU

holiday camps, when they are available, can be an excellent solution to improve autonomy and self-confidence for PKU teenagers.

During adulthood

In adulthood, individuals with PKU face challenges that involve interpersonal relationships associated with the maintenance of their PKU diet, as well as the basic incompatibility between the PKU diet and many lifestyle demands [22]. In women, one of the main behavioral goals is the prevention of an unplanned pregnancy. PKU study subjects have been shown to have more conservative attitudes about sex and contraception than the non-PKU controls. Shiloh et al. [23] showed that men with PKU were rated significantly lower on introversion by their teachers while women with PKU were rated significantly higher on introversion and lower on extroversion than matched controls. This difference between the gender was also reflected in the relationship between measures of dietary control and behavior clusters, suggesting that men and women with PKU respond differently to elevated Phe levels or the stress associated with PKU. This may be the consequence of the pressure put on young PKU females by the medical team in order to prevent the maternal PKU syndrome.

Transitions to adult care

The term “transition to adult care” for children with chronic genetic disorders has often been described narrowly as the transfer of care from a pediatric to adult practitioner with a corresponding change in venue. In the case of many chronic disorders, this transition typically occurs at 18–21 years of age, although the actual age of transition varies widely depending on institutional policies and the desires of the patient and physician.

Due to the lack of adult specialists in metabolic disorders, this type of transition for individuals with PKU rarely occurs in North America. A large majority of metabolic physicians care for both children and adults, although a sizable portion of them are located in children’s hospitals. This presents difficulty in creating an atmosphere that is conducive to adult care. Adults with PKU may be sharing waiting rooms with young children, they may be seen in examination rooms with a childlike décor, and consultation rooms appropriate for discussions with adults are often in short supply.

These factors present a challenge to the health care system, and they need to be addressed as the number of adult patients with PKU and other inherited metabolic disorders continues to increase. In North America alone, 200 PKU patients enter adulthood each year [24]. Since the recommendation is now for blood Phe control for life, the need for focused and appropriate services for adults with PKU is clearly a pressing one.

Transition to self-management

Aside from considerations of change in practitioner and venue, it has been pointed out that the term “transition to adult care” should be considered in the much broader context of transitioning to self-management [25]. As the individual with PKU moves into adolescence, management of the disorder needs to shift from the parent to the child. This process must be facilitated both by the parents and by the health care team.

From early school age onward, practitioners need to begin engaging the PKU individual directly during visits in a discussion of the impact of the condition on their daily lives. They must also begin to develop a partnership with their patient, with increasing responsibility being placed on the individual with PKU to both understand the condition and to manage it. This involves developing increasing independence in maintaining diet records, preparing foods, taking medication, doing blood tests, and monitoring the re-

sults. While parents need to remain involved in a supervisory role, a successful transition requires that they gradually relinquish total control.

This transition process is complicated in PKU individuals by a number of factors that derive directly from the neurocognitive and sociodemographic consequences of the disorder. These include the fact that individuals with PKU exhibit delayed autonomy [26] and poor executive functioning skills [27], which contribute to difficulty in general self-management and such tasks as diet planning and organization specifically. Some adults with PKU experience ADHD and have difficulty forming stable social relationships with partners who could lend support to their efforts to successfully manage their disorder.

As individuals with PKU move into adolescence, decreasing dietary adherence leading to higher blood Phe concentrations causes greater neurocognitive difficulties. It is often difficult to convince adolescents of the benefits of stricter blood Phe control because they do not perceive that they are having symptoms of their disorder, despite the fact that symptoms may be noted by parents or teachers. Adolescents characteristically have difficulty understanding the significance of preventive health measures because of their sense of invincibility. Metabolic clinicians need to be cognizant of all of these factors as they engage the young person in the transition process. Indeed, it can be suggested that even more effort must be expended to facilitate the process in individuals with PKU than in people with other chronic disorders.

Tools that assess neurocognitive functioning on an ongoing basis can be very useful in identifying areas in which young adults are not performing optimally. They also track improvements of blood Phe levels and monitor that they are brought under better control. It is likely that the transition process will be most effective if a specific transition plan is established for each individual with PKU with participation of the individual, parent, and health care team, as opposed to expecting this process to occur automatically as the individual grows older.

Pregnancy and maternal PKU

There are some unique aspects to the care of adults with PKU that are not encountered in caring for children with this disorder. One that is particularly important relates to maternal PKU syndrome [28]. It has been clearly demonstrated that elevated blood Phe levels in the mother are deleterious to the developing fetus in a dose-dependent manner. The higher the blood Phe level and the longer the fetus is exposed, the greater the risk of intrauterine growth retardation, microcephaly, congenital heart disease, and mental retardation.

Education regarding the risks to the fetus associated with poorly controlled blood Phe levels must be initiated with girls at an early age and continued into adult life. It must be emphasized that blood Phe levels need to be well-controlled prior to pregnancy in order to ensure an optimal pregnancy outcome. A comprehensive study of adherence to medical recommendations in maternal PKU identified the importance of social support and positive attitudes (i.e., belief in its efficacy) regarding treatment as the two critical factors in predicting prevention of unplanned pregnancy and adherence to treatment during pregnancy in women with PKU [29].

Since a significant proportion of all pregnancies are unplanned, health care providers should begin talking with adolescent girls at an early age regarding issues of sexuality and contraception. All girls and women who are sexually active should be counseled to use an effective method of birth control. In the event of an unplanned pregnancy, they should be counseled to contact their PKU clinic immediately. Similar issues do not apply when the male parent has PKU, but men and women with PKU need to receive ge-

netic counseling regarding the inheritance of PKU and their risks of having an affected child.

Overcoming adherence barriers

In the United States, many young adults with PKU abandon treatment for their disorder and lose contact with their PKU clinic and their health care team. This may be a result of gradually increasing non-adherence to dietary recommendations ultimately leading to abandonment of dietary therapy. The availability of new therapeutic tools, including medications and large neutral amino acids, may help to keep some individuals with PKU within the system in the future.

An additional barrier to care for many young adults with PKU is financial. Many of the US government-sponsored programs that support clinic visits and laboratory testing and provide funding for medical foods terminate when individuals with PKU are either 18 or 21 years of age. Insurance coverage through parents' employers is lost no later than 25 years of age. Young adults with PKU are often underemployed and in some countries are without access to health care plans [30,31]. Even if they are fortunate enough to have private insurance to cover clinic visits and blood tests, this often does not cover low protein foods which are essential to maintaining adequate blood Phe control.

Social support, positive attitudes toward treatment, and manageability have been shown to predict adherence to medical recommendations in adults with PKU. Subjects who (1) reported having a network or people who believed that they should maintain the diet, (2) expressed positive feelings about the efficacy of treatment and (3) possessed the resources to manage the diet (such as insurance) were more likely to return to treatment and maintain metabolic control. The acronym, SAM, refers to these three factors (social support, positive attitudes and manageability) and serves as a reminder to adults about the need to consider psychosocial factors when returning to treatment [31].

Psychotherapy has also been helpful in improving metabolic control during pregnancy, especially when depressive symptoms are present [32].

It is striking to observe the changes that often occur in adult with PKU who manage to return to metabolic control after having elevated blood Phe levels for a significant period of time. They often report that "the fog has lifted" and that they did not realize how impaired they had been until their levels came under control. They report relief of anxiety, less depression, and a more even temperament. This is often emphatically confirmed by friends and family members.

It is observed in individuals who return to a low-Phe diet that they are able to secure and maintain a job after a lengthy period of unemployment, are able to discontinue medications for depression and anxiety, and they report improvements in their ability to concentrate on tasks at work, home, or school. The goal for health care providers should be to enable patients to maintain adequate blood Phe control throughout the difficult period of adolescence into young adult life and beyond, enabling them to achieve their goals and reach their potential without the neurologic and psychiatric challenges that often accompany poorly controlled PKU.

Non-traditional practice settings in PKU

The dietary management of PKU is complex and time-consuming, requiring knowledge of foods and recipes, cooking skills, continuous food measurement, as well as good organizational and parenting skills. In PKU, many innovative and non-traditional health care programs have been introduced by enthusiastic health professionals that have the potential to ease the burden of dietary

care. The program objectives are wide but include improving the knowledge of the PKU individual and their caregiver, providing practical skills, expanding family social support networks, increasing motivation, and enhancing coping ability. Unfortunately, there is limited scientific evidence for the efficacy of these programs, and although no single intervention could serve as a panacea, some of the schemes could provide a springboard for detailed intervention studies and have the potential to be implemented and embedded into service provision.

Peer support programs for PKU individuals and caregivers

Peer support is an age-old concept, and it is particularly important in PKU communities with limited financial and health care resources. Peer support has been defined as "the giving of assistance and encouragement by an individual considered equal" [33], and it is delivered by someone with personal experience of PKU. Peer support in PKU has included one-to-one sessions with home support workers, self-help support groups, befriending schemes, online computer mediated groups, collective advocacy programs, telephone contact, and summer camps [34,35].

The Maternal PKU Resource Mothers Program matched mothers of children with PKU to women with PKU who were planning a pregnancy or who were already pregnant, with the aim of providing social support, enhancing positive attitudes toward the treatment and ensuring that necessary resources were in place. Women who received the services of a Resource Mother attained metabolic control an average of 2 weeks sooner than women who did not participate in the program [36–38].

Of particular interest is the proliferation of PKU Internet virtual communities through chat rooms, discussion forums, and PKU listservs, where people with PKU or caregivers share experiences, ask questions, or provide emotional support or opinion. Non-moderated social network services, such as MySpace and Facebook, specifically allow individuals to discuss common interests and activities [38]. Although the Internet is being used by thousands of people with PKU throughout the world (there are at least 50 PKU-related groups on Facebook alone), there are some concerns. In PKU, the risks of Internet communication have not been explored, but a systematic review of many health conditions did not find robust evidence to support health risk or benefit [39]. However, lack of evidence does not mean that virtual support groups have no impact. Studies examining self-processes are difficult to undertake in a controlled environment, participants in self-help groups may be a self-selected subgroup, and any effect may be masked by other confounding factors [39].

A form of peer support that has received increasing interest in other health conditions is referred to as "expert patients" or "expert caregivers," who are able to give practical help and support [40]. In PKU, there are no controlled trials examining the outcome of such an approach, but there is one report describing this type of initiative. In a UK study, a "PKU home support worker" with direct experience of caring for a child on a low amino acid diet helped parents build confidence, learn how to prepare low Phe meals, and improve their parenting skills. It was found that caregivers often lacked cooking equipment or had non-functioning kitchen equipment. Specific benefits identified by parents were learning new cooking techniques including the use of unusual food ingredients, receiving ideas for meals or snacks, and help with feeding difficulties in children [41].

Peer support, given through residential events, family retreats, "family to family networks," and mentoring, aim to give caregivers emotional support as well as practical help with parenting skills. Although there are no studies in PKU, research in other conditions has demonstrated that peer support has directly benefited caregivers and has led to improvements in the maternal caregiver's men-

tal health [42] and has reduced feelings of isolation. These studies have also shown that peer support improved parental communication with adolescents [43].

Promotion of self-reliance and self-efficacy

In PKU, parents play a key role in delivering much of the day-to-day care. However, there is now greater emphasis on training children to take an active role in the daily management of PKU and contribute to decision making about their own treatment. The UK Children's National Service Framework states that "children, young people and their families should be supported in the self-care of their condition in partnership with their health professionals" [44]. Involving children with PKU from an early age in their own care through programmed learning and providing theoretical knowledge and practical skills will enable parents to transfer care responsibility and give control to their child with PKU. This will enable PKU children to make informed treatment choices independent of others, which in turn may improve adherence [45].

The long-term success of children's self-management programs has not been evaluated in PKU. Kieckhefer and Trahms [46] have used developmental models as a guideline for parents in teaching their children self-management skills. This consisted of curricula designed for specific ages, with activities that can be used for both groups and individual children. It involves planned progression of responsibility for care from the parent to the child. The parent is initially the manager, then eventually the consultant, and finally the provider of support and guidance only. Similarly, the UK National Society for PKU (NSPKU; www.nspku.org) has produced a teaching skills guide for children called *Let's learn about PKU*. It is designed to aid dietitians and nurse specialists and consists of a number of age-directed and evaluated activities, with every activity being objective driven and accompanied by a comprehensive worksheet or activity description.

In designing self-treatment programs, it important to establish what children wish to know and to ensure there are no information gaps. Delivery of self-management programs is through workshops, clinics, and children's cooking sessions. In our own clinic, we run biannual "PKU schools" for 4- to 10-year-old children with a focus on hands-on activities. Children plan meals, shop for food, measure ingredients, and prepare meals and snacks. In order to maximize school attendance, all activities are highly interactive, creative, and fun. Attendance at "PKU school" replaces a routine clinic visit. Direct practical experience of preparing a low Phe food is essential in order for PKU individuals to gain confidence in managing their diet. Waisbren et al. [34] demonstrated that although a maternal PKU summer camp improved social support networks, it did not promote long-term changes in dietary behavior, possibly because campers had little practical involvement in food preparation.

Blood Phe monitoring

Learning how to take blood samples and understanding the results are essential in the self-management of PKU [10]. In a short-term study of PKU individuals over 1 year of age, these individuals and their caregivers were asked to decide the frequency of blood sampling and had to self-adjust the diet according to blood Phe concentrations. However, this practice led to a consistent rise in blood Phe concentrations in every age group [47]. Even so, it is possible that future availability of home blood Phe monitoring test kits will facilitate better management of PKU through more regular and timely feedback [14], enabling PKU individuals and caregivers to understand their blood results in relationship to recent food intake, thereby improving overall self-management.

Education programs and aids

Education is delivered by all PKU centers, but there is no reported validation and reliable PKU tool that will assess effectiveness of educational outcome. Desired education indicators in PKU should consider knowledge and understanding (including application of knowledge and problem solving skills) as well as self-management (practical skills, appropriate eating, risk reduction, protein substitute taking, and blood taking).

Traditionally, written materials are used to educate individuals and families in all PKU clinics, although it is well established that they are less effective than other educational interventions [48]. In PKU, user involvement appears rare, but it is essential because PKU individuals and health professionals are likely to have differing opinions on educational material content. Recently, a written educational resource for adults with PKU was developed with input from PKU adults. Although it was found to significantly improve short-term knowledge, it did not improve blood Phe concentrations [49]. Other less traditional aids that have been evaluated include audiovisual materials. Evans et al. [50] studied the effectiveness of a cookery DVD and recipe book, mainly in PKU families, and found that one-third of caregivers failed to watch the DVD and almost one-quarter did not even open the recipe book.

Other reported educational interventions include educational summer camps for groups of adolescents and adults. The latter programs have resulted in improvements in knowledge and short-term improvement in blood Phe concentrations [35,51]. However, due to the cost and difficulty in securing health professional involvement, this type of service is unlikely to be accessible to all individuals with PKU.

Behavioral approaches

Changing behavior and attitudes in any population is a difficult task. Although it is important that children and their families understand the condition and its treatment, knowledge is not sufficient to change behavior [52]. Some PKU clinics run programs for children and adolescents to help improve psychosocial well-being. They include discussions or role-plays about coping with the consequences and impact of PKU on day-to-day life (e.g., how to explain the disorder to other people, how to manage the diet at school, dealing with peers, feeling isolated from peers, and being bullied). Other clinics organize activities to increase self-confidence with treatment management, or use social support to encourage adoption and maintenance of specific dietary changes and promote "model patients who practice positive behavior" to help improve self-efficacy.

Cues and rewards for blood testing, although rarely reported, help modify and reinforce behaviors related to compliance. In New Zealand, the MacPhe Reward Scheme in PKU is an ongoing program where children earn points or "bones" in response for returning blood Phe samples and eventually, the points or bones are exchanged for a reward. This has been associated with improved return of blood Phe samples and increased communication with the PKU clinic [53]. It has also been shown, when prompting PKU individuals to comply with blood monitoring, that two prompts (automated phone calls and letters) are more effective than one prompt in inducing compliance with blood sampling [54].

Increased health professional accessibility

In PKU, increased and improved health professional accessibility is being introduced in novel ways, but the availability and success of all approaches is dependent on resources, staffing, and individual or caregiver preference.

Telemedicine

This refers to the provision of clinical services through communications and information technologies (e.g., telephone, Internet, and video conferencing). At least one clinic is piloting the use of the Internet for PKU counseling and reporting of blood Phe results, providing PKU individuals indirect interaction with health professionals. Although the first reports of efficacy are awaited, privacy and confidentiality are key issues that need to be considered, and there may be a lack of immediacy or response compared to active verbal interaction over the telephone [40].

Dietetic home visiting

Traditionally, dietary advice for complex metabolic disorders is given in the hospital clinic. Trying to assess the day-to-day application and understanding of dietary therapy within this environment is difficult; it can lead to an inaccurate impression of parental or caregiver ability to cope with dietary instructions. Parents or caregivers commonly articulate that they adhere to dietary instructions, but a home study investigating the practical dietary management of children with PKU found there were several deficiencies in parental dietary care [55]. It was found through home visiting that mothers of PKU children had poor knowledge of the Phe allocation system, could not calculate from food labels the quantity of food that could be eaten to yield a specific quantity of protein, and could not identify by eye the protein content of pre-measured portion sizes. Many children ate repetitive, simple meals and used few special low protein foods. Some parents had difficulty planning or organizing a suitable low-Phe diet. As a consequence of this, dietetic home visiting has been initiated by some clinics in the UK.

Weekend hospital clinics

Dietary education and practical teaching in traditional weekday PKU clinics is hampered by time constraints, space, and personnel. In weekday clinics, children and caregivers take time away from school or work. In order to improve education and clinic accessibility, Saturday clinics for school-aged children and teenagers (4–16 years of age) have been described [56]. In this circumstance, the waiting area was transformed into a teaching and social network forum for PKU. An independent survey, using a consumer satisfaction instrument designed to measure key criteria selected by caregivers and parent, found that the weekend clinic improved clinic attendance, was more convenient to families, and was associated with high customer satisfaction scores [56].

Improving the convenience of care by easing availability of clinical foods and protein substitute (formula)

In the UK, the traditional system for acquiring special dietary products (patient-prompted prescriptions generated by a medical doctor and dispensed by a pharmacist) was problematic and associated with prescription errors and delays. As a consequence, a prospective 12-month home delivery trial for protein substitute was conducted in patients with inherited metabolic disorders (IMD), including PKU. Fifty percent of subjects used a new monthly home delivery service to receive protein substitute, and 50% remained on the traditional system. The IMD-tailored home delivery service contacted parents and PKU individuals monthly to check stock levels, obtained prescriptions directly from the doctor, and delivered products to the homes of the individuals or parents at the same time each month. The home delivery service was proven to be a more reliable system for dispensing protein substitutes than the traditional system, and it was associated with reduced protein substitute prescription errors. All the study group PKU individuals or parents said the home delivery service was reliable, convenient, and associated with less stress [57]. This service has now been ex-

tended to some low protein special foods in the UK. Prior to this extended home delivery service, many families mistakenly received gluten-free instead of low protein foods from their pharmacist and were issued out-of-date products, and the conventional system was associated with inconvenience and ignorance [58]. Alternatively, in countries like the USA and Canada, where low protein dietary products are purchased by families, it is now easier to order these products directly online from the companies with delivery directly to the PKU individuals' homes.

Conclusion

There is a clear link between metabolic control and the outcome of individuals with PKU, but the management of PKU must take into account the burden of the diet and the fact that having a chronic condition is associated with some psychological disturbances by itself. The psychological management of both PKU individuals and their families must begin from birth and continue to adulthood. Furthermore, the transition to adult care is a process that takes place over many years and needs to be carefully planned to help individuals with PKU become autonomous adults, responsible for their own health care.

Equipping PKU individuals and caregivers with the necessary practical skills, knowledge, and motivation to successfully produce an acceptable low-Phe diet that is compatible with a modern lifestyle is the key to achieving a good treatment outcome at any age. However, this is labor-intensive and PKU health professionals who are commonly hospital based may be unable to address all the day-to-day practical skill requirements of PKU individuals and caregivers, or they may have inadequate resources to meet all their information demands. Therefore, it is increasingly necessary to use peer support programs, to facilitate PKU individuals and caregivers to self-direct treatment, and to help them develop their own strategies to deal with day-to-day problems.

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