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ORIGINAL RESEARCH

Psychosocial Issues in Families Affected by Maple Syrup Urine Disease

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Abstract The primary aim of this study was to ascertain the psychosocial issues faced by families affected by maple syrup urine disease (MSUD). The psychosocial adjustment and quality of life of children with MSUD were also described. Participants included 55 families and their children (ages 5 to 18 years) and teachers. Measures included a MSUD Family Survey, the Behavior Assessment System for Children (BASC) and the Pediatric Quality of Life Inventory (PedsQL). Parents reported via the MSUD Family Survey that the greatest sources of stress were financial and emotional. Many parents reported difficulty interacting with the medical staff and with schools. On the BASC, half of the children fell within the average range in psychosocial adjustment, although there were elevations in scales measuring attention, hyperactivity, and learning problems. On the PedsQL, the mean quality of life scores were closer to children with cancer than to a healthy sample. Despite the emotional and financial burden, parents reported that MSUD has also had a positive influence on their lives, leading to a world-view that is more compassionate and caring.

Keywords MSUD · Psychosocial · Families · Support

Introduction

Chronically ill children are, as a group, vulnerable to behavioral, emotional, and medical problems that can interfere with daily activities and functioning. These challenges of childhood chronic illness also impact the family (Cohen 1995b; Landolt *et al.* 2002; Wallander and Varni 1998). Chronic illness in a child may affect the psychological functioning of parents and siblings, affect employment activities and the economic situation of parents, and affect the functioning of the entire family unit (Cederbaum *et al.* 2001). Parents have an intense burden of providing daily caregiving for their chronically ill child and the illness often involves coping with ambiguities including uncertain outcome and misdiagnosis. When the medical diagnosis phase is prolonged, the long wait for diagnostic certainty can cause extreme psychosocial stress for parents (Clarke-Steffen 1993). When parents are informed of a definitive diagnosis they often experience a wide spectrum of emotions including relief, guilt, shock or anger (Cederbaum *et al.* 2001; Parker 1996). Some parents have likened the diagnosis of a chronic health condition in their child to a "physical assault" (Cohen 1995a). Indeed, following the diagnosis of cancer in their child, parents have reported symptoms similar to those seen in persons with posttraumatic stress disorder (Santacroce 2002). Following the diagnosis of a chronic condition in their

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We dedicate this manuscript to Dean Danner, PhD, who recently passed away. He was a valuable colleague, a wonderful person, and an inspiration to us all.

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child, parents may wonder whether the disease will improve or get worse, ask whether their child will die, and wonder how much they can expect from their child (Clarke-Steffen 1997; Parker 1996). Family members also may experience stress from the lack of information available about the illness from the medical providers who may be unfamiliar with the intricacies of the disorder (Cederbaum *et al.* 2001).

A significant number of families of chronically ill children are affected by financial stress. A chronic illness can add to the financial burden when a child requires medications and special dietary foods (Cederbaum *et al.* 2001; Read and Charbonneau 2004). In addition, marriages can be adversely affected by having a child with a chronic illness, (Midence 1994). Researchers have also found that siblings are significantly impacted by a chronic illness, as they are asked to assume greater familial responsibility and are often given much less attention and reward from their parents (Packman *et al.* 1997; Powell and Ogle 1985). Even though there are multiple stressors for a family with a chronically ill child, these stresses do not necessarily have to be problematic. Some families have reported that dealing with a chronic illness has actually brought the family members closer together (Cederbaum *et al.* 2001; Packman *et al.* 1997; Rehm and Catanzaro 1998).

Inborn errors of metabolism (IEM) are a type of chronic illness that affects children *and* their families. Although individual inborn errors of metabolism are rare, in aggregate approximately 1/1,000 people are born with a metabolic disorder (Enns and Packman 2002). Clinical presentations are variable and include intermittent metabolic attacks (e.g. lethargy, hypoglycemia) multiorgan system involvement, neurological abnormalities, developmental delays, behavior and learning problems (VanZutphen *et al.* 2007), and manifestations of, or actual psychological disorders (Enns and Packman 2002; Packman *et al.* 2006). Patients with metabolic disorders may have behavioral and emotional problems similar to those seen in patients with other chronic disease. For example, the psychological profiles of adolescents with phenylketonuria (PKU) and patients with diabetes mellitus were found to be strikingly similar (Weglage *et al.* 2000). Internalizing problems (anxiety, depressed mood, physical complaints, social isolation) were significantly elevated in both groups. In an assessment of psychological adjustment in children and adolescents with early and rigorously treated PKU (Landolt *et al.* 2002), parents reported a reduction of positive emotions, noting that the children were less happy and confident. In a study examining the impact of galactosemia on quality of life (Lambert and Boneh 2004), it was found that galactosemia had significant impact on the psychosocial aspects of patients' lives, especially interpersonal problems, excessive anger, sleeping difficulties and academic problems.

There are a range of demands that families of children with IEM's face. One study (Cederbaum *et al.* 2001) indicated that the greatest sources of stress imposed on families were financial, fear of death, and the restrictions imposed by the diet. Another study examined predictors of parenting stress in parents of children diagnosed with diverse biochemical genetic disorders (Waisbren *et al.* 2004). It was found that the child's adaptive functioning, parental satisfaction with social support, and difficulty meeting the child's health care needs predicted parenting stress.

Maple syrup urine disease (MSUD) is an autosomal recessive IEM of pan-ethnic distribution with an incidence of 1 in 185,000 births worldwide (1 in 176 births in the Old Order Mennonites of Pennsylvania, USA; Wilcox and Cederbaum 2007). MSUD is caused by a deficiency in the activity of the branched-chain α-keto acid dehydrogenase (BCKD) complex, an enzyme that is responsible for the catabolism of three amino acids, isoleucine, leucine and valine. These essential amino acids are present in the proteins of multiple foods including meat, eggs, milk, fruits and vegetables. Impairment of catabolism leads to an accumulation of these amino acids and their derivatives in the blood and urine resulting in neurotoxicity, and the characteristic maple syrup odor in the urine, respectively. Treatment includes immediate and lifelong dietary restriction of isoleucine, leucine and valine.

Individuals with MSUD can be divided into several categories based on the clinical presentation, enzyme activity and biochemical response to thiamine. The four types of MSUD include classical, intermediate, intermittent and thiamine responsive (Dancis 1974; Wilcox and Cederbaum 2007). The classical form is the most common and severe form. Newborns affected with classical MSUD have 0–2% of normal enzyme activity. They are normal at birth but develop symptoms within 4–7 days of life. If left untreated, seizures and coma ensue, ultimately leading to death. Those who do survive exhibit brain injury, spasticity and profound mental retardation if untreated. Children with intermediate MSUD have a milder neonatal course and approximately 3–30% of normal enzyme activity. When ill, they can present like a child with classical MSUD. Children with the intermittent form of MSUD have approximately 5–20% of normal enzyme activity and show normal early development. Often, intermittent MSUD patients do not exhibit symptoms until 12–24 months of age, and the symptoms are usually brought about by illness or infection. They are asymptomatic between episodes. Children with thiamine responsive MSUD do not exhibit neonatal illness and are similar to individuals with intermediate MSUD. Thiamine-responsive MSUD children are treated with a combined therapy of dietary restriction and thiamine. Regardless of the type of MSUD, immediate treatment greatly decreases the severity of injury and leads to a more favorable outcome.

Dietary treatment for MSUD was developed in the 1960's. At this initial stage, treatment was implemented for neonates already in metabolic crises. While this treatment markedly reduced mortality it had variable influence on morbidity. Since then studies have attempted to identify risk factors associated with cognitive and neurological disturbances such as time of diagnosis, maintenance of dietary control and levels of leucine and its derivative levels in the blood (Kaplan *et al.* 1991; Nord *et al.* 1991). A few studies have documented improved cognitive and neurological outcomes in early-treated and optimally managed children with MSUD (Emory *et al.* 1992; Hilliges *et al.* 1993). The goal of dietary treatment is to maintain branched chain amino acids (BCAA), particularly leucine, within normal limits as studies have shown a correlation between cognitive decline and elevated blood leucine levels (Jurecki 2006; Wilcox and Cederbaum 2007).

Because of the many forms of MSUD, there is variability in diet management. The effectiveness of treatment is monitored by metabolic control, nutritional status, and compliance (Jurecki 2006; Wilcox and Cederbaum 2007). Metabolic control is monitored by checking the plasma amino acid levels, checking the urine for ketones, and tracking dietary protein intake. Nutritional status is monitored by laboratory data, by physical exam, and by monitoring growth. The goal of diet therapy is to maintain blood levels of BCAA within recommended treatment limits while ensuring adequate calories and protein and avoiding nutritional deficiencies (Jurecki 2006; Wilcox and Cederbaum 2007). Thus, the diet must be restricted in the BCAAs, particularly leucine, while delivering enough protein and calories. This requires the use of special medical formulas that include isoleucine and valine (Jurecki 2006; Wilcox and Cederbaum 2007). In addition, protein-free formulas are often necessary in order to ensure an adequate caloric intake.

Management of children with the classic form of MSUD can be frustrating (Wilcox and Cederbaum 2007). Many of these children have died as infants or have major neurologic and cognitive impairment, despite special dietary intervention. Those who survive the neonatal period typically have an IQ averaging in the 70's. Those children with less severe decompensations tend to have better outcomes, as do patients with milder forms (Wilcox and Cederbaum 2007). The outcome can be better if aggressive management is started in the first few days of life. This requires prenatal diagnosis or newborn screening with a short time from testing to referral for care. Patients with MSUD generally do well between acute illness or infections but they are vulnerable to rapid deterioration when they become dehydrated or anorexic (Wilcox and Cederbaum 2007). Longer term care of patients with MSUD involves the use of high-calorie diets with limiting amounts of leucine, isoleucine, and valine. Milder forms of MSUD can normally be managed successfully by dietary intervention; however, these patients remain vulnerable to acute catabolic episodes (Wilcox and Cederbaum 2007).

Compared with the wealth of knowledge that exists regarding the impact of a chronic illness, in general, on family functioning, there is a lack of research on psychosocial issues faced by families of children with MSUD. Thus, the primary aim of the current study was to ascertain the psychosocial issues and concerns of families affected by MSUD. Secondly, we were interested in describing the psychosocial adjustment and quality of life of children with MSUD.

Method

Participants and Procedure

Initially, 118 families from the MSUD Support Group were contacted by letter and informed of the study. Of these, 55 chose to participate, and subsequently, each family was mailed assessment measures along with informed consent. Participants included parents and children ages 5–18. In two-parent families, one parent was asked to complete the measures. Fifty-two out of 118 families completed the MSUD Family Survey (44% response rate); 55 completed the Behavior Assessment System for Children (BASC) Parent Rating Scale (47% response rate) and 24 children and parents completed the Pediatric Quality of Life Inventory (PedsQL; 20% response rate). As part of informed consent, parents signed releases of school information in order to have a teacher complete the BASC Teacher Rating Scale. Thirty-seven teachers completed that measure (31% response rate). In an attempt to increase the overall response rate, the MSUD Support Group listed information about the study in the MSUD Newsletter. All procedures and materials were approved by the IRB at Emory University.

The current study was conducted primarily as a written survey. As a result, participation was anonymous and no data were available on nonrespondents. The generalizability of this study's findings is limited to the population surveyed, i.e., families who are members of the MSUD Support Group and reside in the USA.

Assessment Measures

The MSUD Family Survey consists of 35 closed and open-ended questions designed to provide an understanding of the stresses imposed by the occurrence of MSUD in a family. The questionnaire is a modification of the one originally designed and successfully used to ascertain the stress imposed on families who have a child with a urea cycle defect, an inborn error of metabolism (IEM; Cederbaum *et al.* 2001). While neither version of the survey underwent formal validation, the items for the MSUD Family Survey were reviewed by a panel of experts consisting of two geneticists, two genetic counselors and two pediatric psychologists and their suggestions were incorporated into the final version.

The MSUD Family Survey included demographic variables: age, education, marital status, ethnicity, income, state of residence, occupation, and insurance information. There were 27 close-ended multiple option questions (participants checked as many answers as they felt applied) concerning child and family medical and psychosocial information. The items included questions about their initial reaction to the child's diagnosis, the stresses of having a child with MSUD, impact on finances, changes in their daily activities, career decisions and relationship with their partner, and the amount of stress experienced regarding their child's ability to comply with the diet. We also asked if having a child with MSUD has had a positive effect on them. The survey also included five open-ended questions to allow participants to discuss specific issues. These included questions about experiences and interactions with medical staff and school personnel. We asked participants to express how they maintained their psychological health and social interactions. We also asked "what has having a child with MSUD meant to your life?" To end the survey, we asked for suggestions on how to for improve the care for children with MSUD.

The BASC Parent and Teacher Rating Scales (Reynolds and Kamphaus 1992) cover ages 4–18. There are three forms: preschool, ages 4–5; child, ages 6–11; and adolescent, ages 12–18. The BASC assesses nine clinical areas including hyperactivity, aggression, conduct problems, anxiety, depression, somatization, atypicality, withdrawal, and attention. The scale for teachers also includes learning and school problems. Published internal consistency estimates are high on the parent rating scale (0.82 to 0.91) and exceed 0.90 on all composites on the teacher scale (except internalizing problems; Reynolds and Kamphaus 1992). The correlations between the BASC and other widely used parent and teacher behavior rating scales provide both convergent and discriminant support for the construct validity of both the parent and teacher rating scales (Achenbach 1991).

The PedsQL (child self-report and parent proxy) consists of brief, generic core scales suitable for use with pediatric populations with acute and chronic illness (Varni *et al.* 1999). The PedsQL consists of developmentally appropriate forms for children ages 2–18, and the parent proxy-report is also used for children ages 2–18. The PedsQL is a paper and pencil form which consists of 23 items, 4 scales, and 3 summary scores. The four scales are physical, emotional, social, and school functioning. The summary scores include total scale score, physical health, and psychosocial health. The PedsQL generic scales are designed to enable comparisons across patient populations (Varni *et al.* 1999). Published internal consistency estimates are excellent for proxy and self-reports on the total QOL (a=0.90, 0.88 respectively), physical health (a= 0.88, 0.80) and psychosocial health scales (a=0.86, 0.83; Varni *et al.* 2001). Validity was demonstrated through known group comparisons, and correlations with other measures of disease burden (Varni *et al.* 1999). Items are rated on a 5-point Likert scale, from 0 (never a problem) to 4 (almost always a problem). After transformation, scores range from 0 to 100, with higher scores representing better quality of life.

Data Analysis

The participants' written responses to the multiple option close-ended questions on the MSUD Family Survey were entered into an SPSS statistical program and frequency data were run. For the open-ended questions on the MSUD Family Survey, participants' written responses were transcribed. The transcripts were read repeatedly and content analysis was used to generate a list of recurring, emergent themes, key words, phrases, and a list of common experiences and concerns expressed by participants (Neuendorf 2002). In qualitative content analysis, written text or interviews are categorized and classified. The data are analyzed with a focus on the intentionality and implications of the text (Neuendorf 2002). The themes emerged from the data, but there had to be an element of interpretation by the researcher. The first author examined the participants' answers and grouped them into content domains to compare themes across individuals. As a reliability check, the third author read the participants' answers independently to identify common themes. The two raters discussed the differences until they reached agreement and then coded all the responses for analysis. Agreement was calculated using Cohen's kappa and found to be 0.87 (Cohen 1960).

Mean BASC subscale and composite scores from our data were compared with the BASC normative sample means provided in the BASC manual (Reynolds and Kamphaus 1992). Mean PedsQL subscale and summary scores from our data were compared with the PedsQL normative sample means provided by Varni *et al.* (2002). The participants' responses to the BASC and PedsQL item scores were entered into an SPSS statistical program and frequency data were run. Next, on the BASC, independent sample t tests were used to compare parent and teacher reports. On the PedsQL, paired sample t tests were used to compare children and parent reports.

Results

Description of Sample

Demographic data of the sample are summarized in Table I. The mean age of mothers and fathers was 41 and 43 respectively. For patients the mean age was 11. There were 24 males and 31 females. The sample of participants was mostly Caucasian (70.8%), married (84%), residing in the East (39%) or Midwest (33%) of the USA, and had a bimodal socioeconomic status in the low and middle ranges. We considered the potential bias introduced by the number of families in the study who share a strong belief system. People were asked to list their ethnicity and their state of residence. We looked at all participants' responses in all cohorts and no differences existed.

Table I Demographic Data

Demographic data of the sample	
Age at interview (*n*=51)	
Mother	41 years (range=24–56)
Father	43 years (range=26–57)
Patient	11 years (range=5–18)
Mother's education (*n*=50)	
Eleventh grade or less	26.0%
High school diploma or equivalent	24.0%
One to three years of college or equivalent	24.0%
Four years of college or more	20.0%
Two or more years of graduate school	6.0%
Father's education (*n*=49)	
Eleventh grade or less	28.6%
High school diploma or equivalent	26.5%
One to three years of college or equivalent	24.5%
Four years of college or more	12.2%
Two or more years of graduate school	8.2%
Marital status (*n*=51)	
Single	2.0%
First marriage	84.3%
Divorced	2.0%
Widowed	2.0%
Remarried	9.8%
Ethnicity (*n*=48)	
Caucasian	70.8%
Native American	18.8%
Asian	2.1%
Ashkenazi Jewish	2.1%
Biracial	2.1%
Total yearly income (*n*=42)	
Below $10,000	2.4%
$10,000–$25,999	14.3%
$26,000–$40,999	21.4%
$41,000–$60,000	11.9%
$61,000–$80,000	26.2%
$81,000–$100,000	2.4%
$101,000–$200,000	16.7%
Greater than $200,000	4.8%

Quantitative Findings

MSUD Family Survey

Responses to the MSUD Family Survey multiple options questions are given in tabular form, with the legend to each table restating the question. Parents' initial reactions to learning the diagnosis indicate that concern, fear, and sadness were the most commonly endorsed emotional responses (Table II). As shown in Table II, when asked what stressors having a child with MSUD has placed on their lives, parents indicated that it was an emotional (78.4%) and financial (68.6%) burden to have a child with MSUD. With respect to insurance coverage, 34 out of 48 respondents indicated that they had no insurance and were paying out of pocket for medical care.

When asked about the effects of MSUD on the daily activities of respondents and on career decisions, parents indicated that they had less time for their other children, less time for themselves, and were spending more time on

Table II Reaction to Diagnosis and Stress of Having a Child with MSUD

Reactions	
"What was your initial reaction to hearing your child's diagnosis? (*n*=50)	
Concern	88.2%
Fear	74.5%
Sadness	52.9%
Shock	41.2%
Relief	37.3%
Disappointment	33.3%
Guilt	23.5%
Anger	21.6%
"What stressors has having a child with MSUD placed on your life? (*n*=49)	
Emotional	78.4%
Financial	68.6%
Lack of freedom	58.8%
Interpersonal (with partner)	27.5%
Breakdown of friendships	9.8%

Participants (one parent per family) could be classified in more than one response category.

dietary concerns. Twenty out of 47 parents felt that there was no effect on career decisions yet 12 said that they no longer work outside the home and 9 reported that they chose a less demanding job.

Table III reflects the responses about the effect that a child with MSUD has had on the relationship between partners. Eighteen out of 39 indicated that it brought the family closer together. The most important sources of support for respondents (n=33) were spouses (19 out of 33) and family (5 out of 33). Other sources of support included religious groups, medical personnel, MSUD support group, and friends. Table III also addresses the positive effects that MSUD has had on the family. Many parents felt enriched by the experience and discovered hidden strengths.

Behavior Assessment System for Children

On the BASC Parent Rating Scale (n=55), 29 children fell within the average range on clinical scales. Sixteen out of 55 children were found to be in the at risk range (T score between 60 and 69) in the area of attention and ten in the area of hyperactivity. Ten out of 55 children fell within the clinically significant range (T score ≥70) in the area of attention and seven in the area of hyperactivity. Children who score in the clinically significant range are considered to be in need of intervention.

Table III Impact of MSUD on Relationship with Partner, Sources of Support, and Positive Effects on Family

Impact	
"How has having a child with MSUD affected your relationship with your partner?" (n=39)	
Brought us closer together	32.7%
No substantial effect	14.5%
Caused conflict	12.7%
Better communicators	7.3%
Caused us to separate	3.6%
"What were your most important sources of support?" (n=33)	
Spouse	34.5%
Family	9.1%
Religious group	5.5%
Medical personnel	5.5%
MSUD Support Group	3.6%
Friends	1.8.%
"In what ways has having a child with MSUD had a positive effect on you?" (n=37)	
Taught me my strengths	27.3%
More compassionate	20.0%
Awakened worldview	18.2%
Made me more patient	1.8%

Participants (one parent per family) could be classified in more than one response category.

On the BASC Teacher Rating Scale (n=37), 26 children fell within the average range on clinical scales. Sixteen out of 37 children were found to be in the at risk range in the area of attention, 8 children were in the at risk range for learning problems, and 8 were in the at risk range in the areas of anxiety and somatization. In this sample, 5 out of 37 children fell within the clinically significant range for learning problems. Children who score in the clinically significant range are considered to be in need of intervention. An independent sample t test comparing parents and teachers revealed that teachers endorsed significantly more internalizing symptoms (somatization, anxiety) than parents on the BASC, [$t(36)=3.34$, $p=0.002$].

Pediatric Quality of Life Inventory

On the PedsQL, paired sample t tests comparing children and parent reports revealed statistically significant differences in all domains except school functioning. In the physical [$t(23)=3.03$, $p=0.006$], emotional [$t(23)=2.42$, $p=0.020$] and social functioning domains [$t(23)=2.50$, $p=0.020$], children reported higher quality of life than parents. When compared to both healthy and oncology sample means (Varni *et al.* 2002), the mean total and domain PedsQL scores of MSUD children and parents were closer to the oncology sample than to the healthy sample.

Qualitative Findings: Core Themes from MSUD Family Survey

The main themes that emerged from parents' responses to the MSUD Family Survey were: (1) Financial and insurance concerns; (2) Interactions with medical staff; (3) Meaning to parents' life to have a child with MSUD; and (4) The child's experiences in school. These areas identified by parents are explored below.

Financial Concerns and Health Care Coverage

The vast majority (75%) of families stated that it was a financial burden to care for a child with MSUD because of inadequate or no health insurance. One parent noted:

> It has caused a hardship largely because we had only been married a year and we didn't have chance to become better financially established before being bombarded with extra medical expenses.

Another parent spoke of the financial burden to care for a child with MSUD:

> Because our private insurance was cancelled after diagnosis, our son must receive treatments, therapies, and formula through state or federal programs. In

> order to qualify for these programs family income and holdings must be limited.

Several participants indicated that because they had no insurance, they had years of fighting and struggling to pay medical expenses.

Respondents listed additional items related to caring for their child with MSUD that were not covered by insurance. These included specialty foods and therapies, services outside of school, such as speech therapy, mental health services, and child-care. Many families (46%) indicated that they pay \$100–\$500 per month for items not covered by insurance.

Interactions with Medical Staff

Parents reported both positive and negative experiences with medical personnel. Many parents (60%) reported that coping with the medical staff was a stressful experience for the following reasons: (1) Disrespected by staff; (2) Lack of staff competence or inexperience; and (3) Uncooperative staff. For example, one parent stated:

> My only experience is the fact that I may know more than the doctor does and find myself telling the doctor what to do.

For this parent, finding herself more knowledgeable than the doctor was disconcerting and stressful. In a related vein, another parent commented:

> When my daughter was originally diagnosed as a newborn the doctor and staff at the [local] hospital were not much help and felt that we were "over acting" with the need to get her to [the specialist].

A similar theme was related by another parent who spoke about being disrespected by the staff and lack of staff competence:

> The early years were the worst. It was unbearable to see my babies suffer so much. Some staff unfamiliar with the disorder assume I overreact and they minimize or ignore metabolic symptoms.

Some parents (40%) reported positive experiences such as the following: "Most medical staff...if they don't know about MSUD are eager to learn." Another parent noted:

> In our local hospital, we need to always be on the alert; but they are very willing to contact and work with our special genetic doctors.

The positive experiences of parents speak to the fact that knowledge is power. Confidence in medical staffs' expertise and the care they provide is clearly an important issue to families.

Meaning to Parents' Lives

Parents were asked to tell what having a child with MSUD has meant to their lives. Parents tended to provide multiple responses to this question and the common themes that emerged included both negative and positive feelings, including struggle and stress, becoming more grateful, more compassionate, more caring and patient, and having a shift in perspective and priorities, and a renewed faith in God.

For example, one parent commenting about the struggles and stress of MSUD, felt that the presence and stress of MSUD accompanied any thoughts she had about the future and the desire for more children. Another parent noted that "During illness it is an emotional and financial strain."

Other parents described what they have learned from their child with MSUD and talked about being grateful and more compassionate:

> Having this child has made me aware of each day as a gift. She thoroughly enjoys life and spreads happiness from rising to bedtime...knowing at anytime she could get sick and be gone has made me appreciate even the challenging times.

> I feel that I have become more compassionate to other families with health problems. I enjoy getting together with the MSUD support group. We can really relate.

Several parents reported that MSUD has had a positive influence on their lives, leading to shifts in perspective and priorities and a world-view that is more caring and compassionate:

> It changed my priorities. It made me realize what a fragile and precious gift life is.

Many parents also mentioned that they had become more spiritual or gained renewed faith in God. One parent noted, "I have become a more spiritual person as a result of having a child with MSUD." Another parent stated: "First it was hard when she was in the hospital and they didn't know what was wrong but after we decided to put her in the Lord's hands we felt peace."

Parents described both positive and negative meanings to their lives as a result of having a child with MSUD, ranging from finding personal strength, to struggling with stressors, to becoming more spiritual. This range of meaning, often present in one individual, mirrors the complexity of MSUD.

Child's Experience in School

This complexity is also present in the multiple environments in which a child with MSUD must function and parents must navigate. Parents were asked about their child's experiences in school. Again, parent responses were quite varied and included positive, negative, and mixed experiences (40, 30, 30% respectively). For example, one parent commented, "My son is not treated any different than any other kid at school. The lunch staff is very accommodating."

In a related vein, another parent stated:

> They have been excellent. My daughter is fortunate that she does not need any "special care." The staff have been very helpful and cooperative with listening to us regarding diet and educational concerns.

On the other hand, other parents have had negative experiences. According to one parent, "the school is mostly uncooperative." Another parent noted:

> Her school experiences from kindergarten to 6th grade were very unpleasant. It has left a lasting impression on her.

Other parents reported a mixture of good and bad experiences.

> The staff has had a difficult time trying to comprehend her individual situation. She has had teachers that are caring and want to learn more and unfortunately she has had a teacher who was more indifferent.

These varied school experiences are possibly related to the severity of the MSUD, which impacts cognitive functioning and, in turn, may influence school placement (e.g., special education, private school). A few parents commented on experiencing fewer problems in private schools than in public schools. In addition, the age of the child may influence the school experience. Overall, more positive experiences were reported for the 5–7 year olds, whereas experiences became more negative for older children and teens.

Next, we asked participants to provide suggestions for ways to improve the care for children with MSUD. Parent suggestions included the following: (1) mandatory newborn screening (25%); (2) financial assistance (15%); (3) educate pediatricians, parents, school systems and insurance companies about MSUD (25%); (4) devise a convenient home testing kit to check and monitor levels of leucine, valine and isoleucine (25%); (5) more research to find out if certain conditions (e.g. ADHD, neurological impairment) are associated with MSUD and to come up with a standardized treatment protocol for MSUD (10%).

To end the MSUD Family Survey, we asked, "How do you maintain your psychological health and social interactions?" Parents tended to provide multiple responses to this question and the following themes emerged: Family support, keeping faith, friends, exercise, think positive, professional counseling, and the MSUD Support Group. Several of these themes are illustrated by the following three quotes from parents:

> We have not let MSUD change our lives. We have made it a part of our daily-weekly-monthly-yearly routine.

> Both my husband and myself are very level headed people. We know we have to deal with whatever God and life gives you. We can't change it, so we have to make life the best we can for ourselves, our kids, and the rest of our family. We don't feel mad or sorry for ourselves.

> Prayer, family support. Try to keep the "big picture" in mind without becoming overwhelmed by all the details.

Discussion

The families in this study have a number of psychosocial needs and concerns, and recurrent themes among participants were revealed by this study. Findings from the MSUD Family Survey indicated that families often experience fear, concern, and sadness upon initial diagnosis of MSUD. As one parent reported, "I went through feelings of fear and sadness when our son was first born." Another parent noted that "it was extremely scary initially." Family members also may experience stress from lack of information from medical care providers, who may be unfamiliar with the intricacies of the disorder (Cederbaum *et al.* 2001). Moreover, when the diagnostic phase is protracted, the long wait for diagnostic certainty can cause even more psychosocial stress for parents (Clarke-Steffen 1993). According to one parent, "when she was first born we didn't know where to get help and it was stressful and a struggle. When she was diagnosed they told us at first it was some other deadly disease. No one could direct us to a MSUD specialty hospital. We had to contact a specialist on our own, educate ourselves and then ask our doctors to call [the specialist]."

These emotional reactions to initial diagnosis are similar to those reported by other researchers in families affected by other disorders causing chronic illness (Clarke-Steffen 1993; Cohen 1995a; Parker 1996). Thus, in MSUD, the diagnosis itself raises questions, concerns and fears—What is MSUD? Will the disease improve or get worse? Could I have prevented it? There is also sadness, as parents may wonder how much they can expect from their child; or a feeling of grieving for the loss of a healthy child (Clarke-Steffen 1997; Parker 1996). As noted by one parent in our study, "The future for my child is so uncertain and this is difficult for me to know how to plan for it. What kind of insurance will she have when turning 18 or 21? What will her health and mobility issues be then? Is her kyphosis going to be able to be treated and stopped? How will this effect her future? ”

We need to be mindful of the many demands and psychosocial issues that families of children with MSUD face and what is *unique* about MSUD *as a chronic illness*. MSUD [and other inborn errors of intermediary metabolism (Cederbaum *et al.* 2001)] are characterized by: acute metabolic decompensation(s); the possibility of neurodevelopmental delays; treatment by nutritional manipulations and supplements; and, ultimate treatment by liver transplant. There is a lifelong strain of dietary management as well as cognitive disabilities. The patients face ongoing metabolic decompensation and a risk of death with decompensation. There are multiple visits to hospitals and physicians. The diagnosis can be in the newborn period or very early infancy; therefore, it is a life-long process, as opposed to cancer, diabetes, or even other inborn errors (Packman *et al.* 2006), which may strike an adult. Conventional treatment does not cure the disease and the treatment may not be effective. There is a lack of control over the treatment parameters when the child gets older (VanZutphen *et al.* 2007). If a child has a chronic disease and has to take a medication, a parent or physician can say “you are taking this medication to treat this disease.” But in this case the treatment is “you can’t eat what other kids eat” and this is very different and difficult to explain to the child. For all of the above reasons, and given the paucity of such literature in inborn errors, MSUD is an excellent paradigm for rigorous study of the psychological consequences and effects of a diagnosis of an IEM in the patient and the family.

Emotional stress as a consequence of the occurrence of MSUD was reported by 78.4% of parents. The quantitative results from the BASC and PedsQL help elucidate these issues and enrich our MSUD Family Survey findings. Approximately half of the children with MSUD fell within the average range on the clinical scales of the BASC (parent and teacher rating scales). It is noteworthy that both parents and teachers reported elevations on scales measuring externalizing behaviors (attention, hyperactivity), and teachers noted learning problems. More specifically, by parental report, 10/55 children fell within the clinically significant range in the area of attention problems and 7/55 in the clinically significant range in the area of hyperactivity. By teacher report, 5/37 children fell in the clinically significant range in the area of learning problems. In addition, teachers reported significantly more internalizing symptoms (anxiety, somatization) as compared to parents on the BASC. One possibility for this finding is that, in an attempt to fit in socially among their peers, children with MSUD minimize acting out behavior and manifest more internalizing symptoms while at school. It is possible that the restrictions of MSUD and the diet are particularly stressful for the child in the school setting, since children manifest more anxiety and somatic complaints in school than at home. A number of our observations have been separately and disparately alluded to in studies of PKU (VanZutphen *et al.* 2007; Weglage *et al.* 2000) and galactosemia (Lambert and Boneh 2004).

Health related quality of life issues relate to the everyday functioning of children, including their physical functioning, emotional and social well-being, behavior, school performance, self-esteem, and family life (Landgraf and Abetz 1998). The understanding of the impact of pediatric chronic illnesses such as MSUD on quality of life is an important advance in our appreciation of the many psychological sequelae and social-emotional factors that are impacted by a child’s heritable metabolic disorder such as MSUD. Consistent with other studies that utilize the PedsQL or other quality of life measures (Lambert and Boneh 2004), there was a discrepancy between child and parent reports. In our study, children reported a higher quality of life than parents in all domains indicating, perhaps, the differences between children and parents in their understanding of MSUD and the sequelae of the condition. It is important to note that the mean scores of children with MSUD, reported both by parents and children, were closer to children with cancer than healthy samples (Varni *et al.* 2002). Thus, even though there may be differences in perception between parents and children, the responses of both groups provide evidence of the significant impact of MSUD on the child’s quality of life.

Taken together, the results from the MSUD Family Survey, BASC and PedsQL help us better understand the emotional burden experienced by families affected by MSUD. Possible factors contributing to family stress may include: coping with a strict diet; the strain of daily activities; cognitive disabilities; externalizing behavior in children (attention, hyperactivity, learning problems) as well as negative school experiences; and, poor health related quality of life issues related to everyday functioning in physical, emotional, social, psychosocial, and school domains.

Parents also reported, by the MSUD Family Survey, that having a child with MSUD is a source of considerable financial stress. In our sample, financial stress as a consequence of MSUD was experienced by 68.6% of parents. Moreover, the majority of participants had no insurance or their insurance was inadequate to cover necessary specialty foods and therapies.

Clearly, another stressor for families affected by MSUD relates to dealing with medical personnel. Much literature on parent-physician interaction focuses on conflicts in the relationship (Kazak *et al.* 2003; Tellerman and Medio

1988). It is important for health care providers to understand that parents may react to a diagnosis of MSUD with fear, concern, and sadness. Understanding parents' fear is crucial in assisting them to understand the diagnosis and cope with it. In addition, parents noted several problems related to medical staff competence—feeling disrespected by staff, dealing with incompetent staff or with uncooperative medical personnel. Families of children with MSUD want and need to be taken seriously by medical care providers and to feel confident in the care provided to their child. Researchers are beginning to advocate the practice of family systems models in pediatric health care to help manage conflicts and develop trust in relationships (Kazak *et al.* 2002). Such an approach may be especially helpful with families affected by MSUD.

In our study, many parents also expressed difficulties with schools. Children with MSUD are likely to have cognitive difficulties as well as less than optimal quality of life even with good dietary control. School personnel may have little or no knowledge of, or experience with, MSUD. It would seem that lack of knowledge on the part of school personnel about the effects of MSUD on a child's cognitive and behavioral functioning may contribute to family stress. It may be necessary for professionals at the metabolic clinic to educate teachers and school personnel about the child's special needs (Read and Charbonneau 2004). The help of the school nurse may be enlisted to assist with these efforts. In addition, a clear letter carried by the parents and child spelling out acute care needs (diet management) and contact numbers (family, geneticists, primary physician, hospital) would be helpful for families.

While it is clear that MSUD places a financial and emotional burden on families, parents also reported that MSUD has had a positive influence on their lives, leading to a shift in priorities and a world-view that is more caring and compassionate.

Conclusion

The findings from this study can be used to alert health care professionals to the importance of continued education in the symptoms and treatment of MSUD. Families want to be taken seriously by medical personnel and to feel confident in the care given to their child with MSUD. In addition, given the stress and worry that families experience, the results of this study can guide mental health professionals to support families in aspects of needs such as financial and health care coverage resources, time management, child care, and, dietary planning. Confidence in the expertise of medical care personnel and the care they provide is clearly a salient issue to families of children with MSUD, and can lead to a stressful, or to a satisfactory and comforting experience. Finally, the results of this study highlight the complexity of the psychosocial affects of MSUD, and detail the various stresses that families face. While MSUD clearly places a major burden on families, parents reported that it can also have a positive impact and allow one to be more compassionate, caring, and appreciative of life and family.

The findings from our study can be used to build stronger interdisciplinary health care teams, to formulate potential systems changes, and to support families in their efforts to provide care to these children. It is important to involve geneticists, genetic counselors, nutritionists, psychologists, and individuals who have expertise in insurance coverage and social work. Other means of support include child and/or family therapy and support groups (e.g., MSUD Support Group). To help families deal with the stressors associated with MSUD it is essential for health care professionals to validate the feelings of children and family members in order to provide interpersonal support, reassurance, and encouragement to maintain hope. Eliciting the parents' emotional responses is critical to reaching treatment decisions that will serve the child's long-term needs.

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