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Inborn errors of metabolism: Psychosocial challenges and proposed family systems model of intervention

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ABSTRACT

Inborn errors of metabolism result in psychosocial crises that challenge individual and familial modes of functioning across the life cycle. Increased stress, mood disorders, interpersonal challenges, decreased quality of life, and grief reactions are all common for patients and their families. To effectively care for these patients, a holistic approach to their care, which incorporates their social context, is essential. Patients and their families need support as they focus on immediate practical demands, grieve over illness-related losses, and reorient future expectations. A family systems based model provides a flexible and individualized approach to care that allows for optimal psychosocial adjustment throughout the disease process.

1. Introduction

Inborn errors of metabolism are chronic diseases that can develop from infancy through adulthood and affect the entire family system [1]. Clinical presentations and symptom profiles are varied and can include: episodes of metabolic decompensation, neurological symptoms, multi-system organ involvement, developmental delays, learning disabilities, and behavioral problems [2]. The medical aspects of inborn errors are well studied; however, less attention has been given to their psychosocial effects. Many individuals with inborn errors experience psychological symptoms secondary to the pathophysiology of the disease or as a result of psychosocial stressors inherent in living with chronic illness [1, 3]. Similarly, parents and families experience psychological distress as the result of having a loved one with an inborn error [4]. Unfortunately, the lack of research on psychosocial issues related to inborn errors results in a dearth of treatment interventions for patients and families. The purpose of this article is to highlight psychosocial issues experienced by individuals living with inborn errors, draw attention to the importance of assessing the fit between family variables and the demands of the disease over the lifecycle, and propose a family-based treatment model to facilitate coping.

The authors conducted a literature search using psycARTICLES and Psychology and Behavioral Sciences Collection databases with the search terms: "psychological," "social," "cognitive," "emotional," "psychosocial," "pediatric," "inborn errors of metabolism," "metabolic disorder," "parent," "sibling," "family," and specific disease names. The results were cross-referenced with a PubMed search using the same search terms and yielded a total of approximately 100 journal articles.

For the purpose of this article, dividing inborn errors into two categories based upon the demands of the disease provides a framework for discussing psychosocial issues. *Category 1* disorders are typified by symptom free intervals with episodic acute metabolic derangement, often triggered by stressors such as intercurrent illnesses, catabolism, and food intake. *Category 1* disorders encompass diseases characterized by the accumulation of toxic compounds such as amino acidopathies, organic acidopathies, and urea cycle disorders, as well as disorders of energy metabolism, such as fatty acid oxidation defects and mitochondrial diseases. Many of the *Category 1* disorders have treatment options, which include removal of the toxin by diet, extra-corporeal procedures, and pharmacological detoxification [5], as well as preventative measures to avoid energy impairment. *Category 2* disorders, characterized by organ system involvement and persistent symptomatology independent of stressors, are typically progressive with a poor prognosis and include conditions such as lysosomal storage diseases (LSDs) and peroxisomal disorders. While treatment options exist for a minority of *Category 2* diseases, treatments are often invasive (e.g., enzyme replacement therapy) and of limited efficacy [6].

2. Psychosocial issues

Patients with either intermittently acute or progressive metabolic disorders may experience psychological problems similar to those seen in other chronic illnesses. Emotional distress, internalizing problems (e.g., anxiety, depression), social, behavioral, developmental, financial, and relational issues are common to patients living with

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Table 1
Commonly cited stressors for patients and families with inborn errors of metabolism.

Sample	Results	Reference
Category 1		
Parents of children with inborn errors	49% of parents endorsed financial stress as a result of child's disorder; 19% loss of friends, 92% emotional stressors; 54% lack of freedom; 48.5% mental; 36% interpersonal; 66% burden of medication management	[4]
Parents of children with MSUD	78.4% emotional burden; 75% inadequate/ no medical insurance; 68.6% financial burden; 60% coping with medical staff; 58.8% lack of freedom; 27.5% interpersonal (with partner); 9.8% breakdown of friendships	[8]
Category 2		
Adults with Gaucher disease	25% patients endorsed moderate to severe financial hardship due to IEM; 22% indicated moderate to severe effect on social life and relationships; 11% reported IEM to have a considerable or extreme effect on ability to do their job	[9]

inborn errors [1]. Psychological reactions specific to the demands of the disease, on the other hand, vary considerably between the two disease categories. Both general and category-specific psychosocial issues are critical to consider when working with patients and their families.

2.1. General psychosocial issues similar to all inborn errors

2.1.1. Common stressors

The stress of living with a chronic illness is well-documented, as is the extreme stress endured by parents of chronically ill children [7]. Stressors prevalent in individuals living with inborn errors include: emotional, social, financial, medical, and lack of freedom [4] (Table 1).

2.1.2. Common psychological reactions

With the myriad of stressors related to inborn errors, it follows that patients and their families often experience significant psychological distress. (See Table 2 for examples). Of note, the relatively few studies examining the psychological reactions of individuals with inborn errors focus on only a handful of metabolic diseases.

Table 2
Common psychological reactions experienced by patients and families with inborn errors of metabolism.

Sample	Results	References
Patients		
	Category 1	
Individuals with galactosemia	Elevated interpersonal problems, excessive anger, academic problems, and sleep difficulties	[18]
Adults with galactosemia	39% experienced depression and 63% experienced anxiety	[19]
Individuals with galactosemia	Compared to healthy peers, lower HRQoL[a], more behavioral problems, lower adaptive skills, more internalizing behaviors	[20]
Children with MSUD	Elevations in scales related to inattention and hyperactivity on BASC[b]; PedsQL[c] scores closer to children with cancer than healthy children	[8]
Adults with PKU	Increased incidence of depression and anxiety	[13]
Children with PKU	Significantly elevated rates of anxiety, depression, physical complaints, and social isolation	[14]
Children and adolescents with early treated PKU	Children were less happy and confident, had less positive emotions	[21]
	Category 2	
Adults with Fabry disease	Lower scores in categories of Physical, General Health, and Vitality on HRQoL[d]	[15]
Adults with Fabry disease	Prevalence rate of depression is 43% in FD patients	[16]
Adults with Fabry disease	60.7% of participants with FD expressed excessive somatic complaints, 39.3% displayed depressive symptoms, 46.6% appeared to experience emotional distress and increased physical symptoms under stress as measured by MMPI-2[e]; FD patients report physical and emotional symptoms similar to chronic pain patients	[17]
Adults with Gaucher disease	25% endorse depression, 35% report anxiety/worry, and 45% report a better outlook on life than others they know	[9]
Adults with Gaucher disease	29% of participants with GD displayed depressive symptoms, 36% appeared to feel generally overwhelmed, and 39% expressed excessive bodily concerns as measured by MMPI-2[e]	[3]
Adults with Gaucher disease	Lower scores in categories of Physical, General Health, and Vitality on HRQoL[d]	[12]
Parents		
	Category 1	
Parents of children with galactosemia and PKU	Parents report lower HRQoL[f] than parents of healthy children and children with other chronic conditions	[10]
Families/parents of individuals with galactosemia	Compared to families of healthy persons, parents experience lower HRQoL[d], emotional, social, and cognitive functioning, and problems with communication, worry, daily activities, and family relations	[20]
Parents of children with MSUD	More compassionate and caring world-view; Parents report on their child's school experience: 40% positive, 30% negative, 30% mixed with older children having more negative experiences	[8]
Parents of children with metabolic diseases	Emotional support was protective for parental HRQoL[f]; loss of friendship was risk factor; medical and socio-demographic variables were not predictive	[22]
	Category 2	
Families of children Gaucher disease	Strengthened family and social relationships and positive outlook	[9]
Parents of children with biochemical genetic disorders	32% endorse significant elevations in parenting stress	[23]
Parents of children with metabolic diseases	63% "made me more compassionate;" 25% "made me an activist;" 67.5% "taught me my strengths;" 49.5% "made me more patient;" 43% "awakened my world view"	[4]

[a] HRQoL (health related quality of life) as measured by the Medical Outcomes Survey, Short Form Health Survey (SF36v2) for adults and the Pediatric Quality of Life Inventory (PEDSQL) for children.
[b] BASC-2 (Behavior Assessment System for Children-2) is a self and parent report measuring internalizing and externalizing problems, behavior symptoms, and adaptive skills.
[c] PEDSQL (Pediatric Quality of Life Inventory) measures social, emotional, school, and physical aspects of quality of life in children.
[d] HRQoL as measured by the Medical Outcomes Survey, Short Form Health Survey (SF36v2).
[e] MMPI-2 (Minnesota Multiphasic Personality Inventory-2nd Edition) is a self-report measure of personality characteristics.
[f] HRQoL as measured by the TNO-AZL Questionnaire for Adults' Health Related Quality of Life (TAAQoL).