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Developmental and psychosocial issues in CF

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Synopsis

Cystic Fibrosis (CF) is a multi-systemic life-limiting genetic disorder, primarily impacting respiratory functioning. Most patients with CF are diagnosed by 2 years of age, and the current median predicted survival rate is 37.4 years old, with 95% of patients dying from complications relate to pulmonary infection. Given the chronic, progressive and disabling nature of CF, multiple treatments are prescribed, most on a daily basis. Thus, this illness requires children, with the aid of their families, to adopt multiple health-related behaviors in addition to managing more typical developmental demands. The morbidity and mortality factors pose cognitive, emotional and behavioral challenges for many children with CF and their families. This article will apply a developmental perspective to describing the psychosocial factors impacting psychological adjustment and health-related behaviors relevant to infants, preschool and school age children, and adolescents with CF. Topics particularly pertinent to developmental periods and medical milestones will be noted, with clinical implications highlighted.

Keywords

Cystic Fibrosis; chronic illness; adherence; quality of life; coping

Cystic Fibrosis (CF) is the most common life-limiting genetic disorder of Caucasians, affecting approximately 30,000 individuals in the United States(1). It is an autosomal recessive disorder resulting from aberrations in the gene that encodes the CFTR protein, thereby causing abnormal ion transport throughout the body. In the lungs, this leads to problems with mucous clearance which subsequently sets the stage for chronic lung infection and inflammation. Respiratory symptoms are experienced by nearly every patient. Gastrointestinal consequences include exocrine pancreatic insufficiency (in an estimated 90% of individuals), which sets the stage

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for CF-related diabetes (CFRD) in an estimated 50% of adults over the age of 30 years old. Other gastrointestinal effects include poor nutrient absorption (especially for fat), biliary cirrhosis, bile duct proliferation and excessive absorption of fluid, increasing the risk for intestine obstruction. In fact, 20% of patients with CF have meconium ileus within the first 24 hours of life. More early symptoms indicative of CF include respiratory infections (most often cough or pulmonary infiltrates) and failure to thrive. Additional symptoms that occur across the lifespan include chronic sinusitis, nasal polyps (present in 25% of patients), and late onset puberty. Infertility is present for nearly 95% of males due to absence of the vas deferens and for 20% of females due to ion transport issues in the genitourinary system, such as abnormal cervical mucus(2). Pain is common throughout the disease course(3). Whereas 50 years ago most children with CF died before 6 years of age, in 2007 the median predicted survival rate was 37.4 years old. 95% of patients die from complications relate to pulmonary infection, with females more at risk for mortality than males(1).

Children suspected to have CF are diagnosed by identification of clinical symptoms and analysis of sweat chloride values, i.e. “the sweat test”. Testing sometimes has to be delayed until the infant produces sufficient sweat for the procedure. Currently, more than 70% of patients with CF are diagnosed by 2 years of age, with some children diagnosed pre-natally. Due to newborn screening programs (NBS), more children with CF are being diagnosed during the newborn phase. Evidence suggests that NSB programs are effective in promoting early health care for affected infants, corresponding with improved outcomes in nutritional status and decreased hospitalization(4).

Given the chronic, progressive and disabling nature of CF, multiple treatments are prescribed, most on a daily basis. Maintenance of lung health is of primary concern and pulmonary treatments include airway clearance techniques (ACT) (e.g., coughing, breathing exercises, and chest percussion) and acute and chronic antibiotic treatment. Gastrointestinal treatments include pancreatic enzyme replacement and vitamins. High-caloric dietary intake and vitamin supplements are often necessary to offset the poor gastrointestinal absorption of fats and nutrients. Patients with CF are recommended to consume between 110–200% of the dietary reference intakes for energy (DRI) for healthy individuals to enhance nutrition and growth (5). Thus, this illness requires children, with the aid of their families, to adopt multiple health-related behaviors in addition to managing more typical developmental demands. The comprehensive nature of CF experience and treatment results in CF really being a “family” diagnosis.

Despite the enormous treatment burden and shortened mortality, individuals with CF and their families have been shown to be tremendously resilient, with the majority of patients and parents reporting a high quality of life and normative levels of psychopathology(6). Nonetheless, the morbidity and mortality factors are understandably challenging for many children and their families, and there is a subset of patients and families for which more significant psychological distress is noted. This article will apply a developmental perspective to describing the psychosocial factors impacting psychological adjustment and health-related behaviors relevant to infants, preschool and school age children, and adolescents with CF. Topics particularly pertinent to each developmental period will be noted. In addition, psychological factors related to noteworthy medical milestones will also be examined in respect to their interface with and impact on psychosocial functioning. Clinical implications and recommendations will be presented throughout.

PERI-NATAL

Attachment, the reciprocal bonding relationship between the infant and the parent which evolves based on the mutual connection of their dyad, is a primary task of this developmental

stage. Both the parent's and the infant's mental representations and behaviors are involved in the attachment process. The parent-child relationship is a critical context for the developing infant, and the quality of attachment predicts important child psychosocial factors such as emotional and behavioral regulation, social skills and the ability to cope with stress management. Parental distress can have negative implications for attachment, particularly when coupled with parental depression and anxiety(7).

The attachment period often coincides with the time of CF diagnosis. Understandably, the diagnostic process is an emotionally challenging one. Even prior to a definitive CF diagnosis, parents of infants with positive CF screens during NBS report high levels of depressive and anxious symptoms, frequently accompanied by hypervigilence such that parents misinterpret common newborn behaviors as evidence of CF. Negative emotions such as worry, sadness and guilt due to the hereditary component of CF are common(8). Worse coping with a positive screen has been found when parents were not knowledgeable about the NBS process, had little knowledge about CF and were experiencing more general adjustment issues related to the newborn period (significant sleep deprivation, adjusting to role of new parent). In addition, parents' distress was reported to be amplified when the medical team communicated the results of the screen in an impersonal fashion and before the infant was old enough to undergo sweat test (resulting in extending the waiting period)(8). Once a CF diagnosis is confirmed, parents typically continue to experience fluctuating states of psychological distress and normalcy as they take on the role of medical parent(4), and may be particularly vulnerable to depressive symptoms while their infants are still only a few months old. Glasscoe and colleagues(9) studied the mental health of parents of infants with CF and reported that both mothers and fathers of infants less than 9 months old had higher relative risk of scoring at or above the clinical cut-off for mild depression (on the Beck Depression Inventory) compared with parents of age-matched healthy controls (relative risk 2.6 and 2.26, for mothers and fathers respectively). No elevated risk was found in parents of older infants.

Despite this risk of heightened distress in parents during the initial attachment period, there do not appear to be higher rates of maladaptive attachments between infants with CF and their parents, again highlighting the resiliency of families with CF(4,10). However, when maladaptive attachment does occur, it has been found to have a negative impact on the health status of infants with CF. Infants with CF who demonstrate problematic attachment styles have been found to have significantly poorer nutritional status and lower BMI(10). Apart from the positive findings related to general attachment patterns, other research has found differences between families with CF and healthy controls in specific parent and child behaviors. For example, one study using direct observation to explore differences in interpersonal behaviors of children with CF between the ages of 12 and 24 months and their parents versus healthy dyads found parents of children with CF demonstrated more controlling, serious and less encouraging behaviors while their children displayed more whining and less responsivity to parent behaviors(11). Thus, even in the earliest stages of development, the toll of CF may begin to influence family interactions.

Clinical implications

Screening for parent mental health concerns is critical during early infancy in order to provide appropriate intervention and maximize parental ability to engage meaningfully and positively with their child. Paying close attention to parents' emotional responses to the CF diagnosis such as guilt or worry is important because persistent negative emotions may have significant effects on both child and parent mental health. For example, a study of parents of children with CF in ages ranging from 5–12 years old found that over 40% of the parents in their sample blamed themselves for their child's illness as a coping strategy. Use of self-blame was significantly associated with worse emotional adjustment for both the children with CF and

their parents(12). Providing education and support during the early diagnostic period may ameliorate some of these unhelpful reactions thereby preventing long-term negative correlates (13).

In addition, early signs of problematic interactions between child and parent should be a cue to closely track important physiological outcomes and to look more closely at how health behavior patterns are unfolding. Helping parents implement developmentally-appropriate effective routines around both general daily activities as well as CF-specific treatment tasks can promote positive reciprocal relationships and increase enjoyment of time spent together. These types of interventions may be particularly important for treatment-related activities which are shown to have poor adherence later in development. For example, Grasso and colleagues reported that using music during ACT in infants and toddlers led to parents rating both their own and their child's enjoyment of the time better and made the time go more quickly (14).

EARLY CHILDHOOD: Preschool

During the preschool period, developmental issues related to expanding language skills, cognitive development in areas such as understanding causality and assessment of ability to control environment, and emotional/behavioral regulation development may be of particular relevance to the experience of CF. Developing language skills helps the child process and express their experiences so that parents and health care providers can have a better understanding of the child's cognitive and emotional events. While much research has tied children's causal attribution to Piagetian stages, with young children attributing illness to magical or superstitious factors, recent research suggests that preschool children may have a more sophisticated understanding of illness which also incorporates biological factors(15). In fact, in the one study that looked directly at causal attributions in a CF sample, over one-half of the 4–6 year old children with CF knew that they had been born with the illness and only 1 out of the 17 preschoolers studied stated they were being "punished" with their CF(16). However, few knew what the various treatments were for(16). The preschool child is also still developing accuracy in understanding which events can or can not be controlled, which has significant implications for the young child with CF who may be in a myriad of stressful environmental situations beyond their control such as medical procedures and treatments(17). The young child with CF may exhibit extreme behavioral reactions in order to attempt to escape these procedures, and may develop heightened aversion for future medical events.

The interface of behavioral self-regulation and CF-related tasks is particularly noteworthy in this age range when preschool children are already contending with increasing awareness of behavioral limits while parents are developing strategies to enhance compliance. Even when children have mild disease and low levels of symptoms, treatment burden is significant: daily nutrition goals, enzyme supplementation and ACT are recommended in order to preserve growth and lung health. The increased opportunities for parent/child conflict may alter parenting strategies such that parents may become either more authoritative or "harsh" (particularly for health-related behaviors deemed essential for survival) or more permissive due to parenting resources stretched thin by the chronic illness, a "choose your battles" approach, or overprotection. These additive behavioral demands associated with CF treatment can challenge the emotional resources of children and parents and can have negative implications for child and parent mental health, general family functioning and health-related outcomes. There is little research exploring general psychosocial functioning in young children with CF. However, Ward and colleagues(18) recently published the results of a study comparing parent-reported behavioral functioning of preschoolers with CF with normative data. While elevations in child internalizing or externalizing mental health issues were not found, nearly half of the children with CF were found to have moderate to large sleep and/or

eating problems, and 40% of the children had poor compliance with ACT. Thus, while not appearing to have significant psychological impairment, these preschoolers with CF did struggle with health-related processes and behaviors.

Problematic mealtime behaviors are a particularly salient health-related concern for children with CF because they are at high risk for poor growth due to chronic lung infection and dietary fat malabsorption. Nutritional status, in turn, is related to lung functioning, health complications, and morbidity in CF. While nutritional guidelines for children with CF recommend eating between 110–200% of the DRI, studies of infant, toddler and preschoolers report typical consumption of only 100% of DRI with fewer than a quarter of the children achieving the minimum recommendation for children with CF(19–20). As might be expected given the sense of urgency parents feel and the higher demands placed on the children, mealtimes with preschoolers with CF have been shown to be more problematic than in healthy families. Children with CF demonstrate a higher frequency of behaviors that interfere with eating such as crying and whining, delaying meals by talking, spitting out food, and leaving the table(20–22). At the same time, parents of children with CF engage in behaviors such as increased coercion, commands, physical prompts and actual feeding of preschools compared to a healthy sample(22). Perhaps not surprisingly, parents often cite mealtime as a particular concern, and report feeling that they have little control over their children's eating patterns (23).

While CF related eating concerns persist throughout development, assessment and intervention during early childhood may change the trajectory of maladaptive behaviors and interactions. In general, behavioral problems in children in this age-range are best treated through behavior modification. A recent randomized clinical trial of behavioral modification involving toddlers and preschoolers with CF found an increase in average daily caloric intake of approximately 850 kcals, corresponding to 120% of DRI. This was significantly better than a treatment-as-usual control condition in which the children's caloric intake declined during the same period. The gains found in the behavioral treatment group were maintained at 3 and 12 month follow-up. The intervention consisted of 6 weekly individual sessions during which parents received nutrition counseling and training in behavioral modification principles. Specific behavioral techniques highlighted included active praising of desired eating behaviors, ignoring noneating behaviors, setting time limits for meals, using successive approximation to determine weekly goals and providing tangible reinforcement for goal achievement(24).

The management of developmental and treatment-related concerns for the preschooler may have negative implication for broader family interaction patterns as well as the adjustment of other family members. For example, Spieth and colleagues(22) compared mealtimes of families of a preschool child with CF to families of children without CF. Relative to the healthy control families, the families with a child with CF had greater deficits in family functioning in areas such as communication, emotional expression, interpersonal involvement and appropriate behavioral expectations and enforcement. Greater marital role strain and decreased home recreation time have also been reported in families caring for a preschool child with CF (25). There is also evidence that parents of preschoolers with CF are at risk for problematic psychosocial functioning. For example, in the study by Ward and colleagues, parents of preschoolers with CF reported elevated levels of depression (33%), anxiety (16%) and stress (34%)(18).

Siblings in the household may also be impacted. Research across chronic illnesses have shown that the presence of a child with chronic illness in the family has a negative impact on siblings, particularly in the areas of peer activities and psychological functioning(26). While sibling psychosocial functioning has not been studied in CF, research has examined differences in how parents treat the child with CF compared with a healthy sibling. A study comparing parenting

practices toward sibling dyads in which the younger sibling had CF versus sibling dyads of 2 healthy children found greater discrepancy in patterns of differential treatment in the families with CF. Mothers spent more time with the younger sibling who had CF in both mealtimes and playtimes. In addition, mothers rated the quality of their time with their ill child as extremely positive, but reported as much negative time as positive time during interactions with their well child despite no evidence that these children had worse behaviors(27). The strong emotional reactions of having a child with a life-limiting illness may promote more positive feelings toward that child and more negative parenting relationships with well children. Beyond the effects this differential treatment may have on the sibling's adjustment, the quality of the sibling relationship may be negatively affected, which may have long-term social implications for both children(28).

Clinical implications

Given that the young child's experience with medical issues impacts longer-term psychosocial and biological outcomes, it is imperative that children be given developmentally-appropriate but accurate information about their illness even during these early ages. The findings that children may be able to understand illness causality at a more sophisticated level than previously thought is encouraging, and should be capitalized on in helping children understand the relationship between their illness and the resulting daily treatments and medical procedures. Interventions to maximize coping with early distressing CF-related experiences is also important both for current and future interactions with health care provision, and research suggests that adequate pain management and non-pharmacologic interventions such as distraction can be helpful in decreasing aversive responses to procedural anxiety and pain (17).

Helping families maintain healthy family dynamics despite treatment burden is a priority with children at this age. While most research has applied behavioral therapy to dietary recommendations in this age group, behavioral strategies can be applied more broadly to improve adherence across CF tasks(29). Insuring that parents are knowledgeable in behavioral management strategies is critical in order to positively impact their young child's health behaviors in ways that promote prosocial behaviors and increase parental self-efficacy. Inquiring about the functioning of specific family members as well as overall family interaction patterns can also identify areas for clinical intervention. One positive impact of CF on family relationships is that parents of a child with CF have been shown to spend more time with that child in play and less time in chores compared with parents who have healthy children, perhaps reflecting prioritizing the resource of time when confronted with a life-limiting disease(25). Validating the importance of prioritization with parents in conjunction with more effective parenting strategies may help them redistribute some of their limited resources of time and energy to self-care, marital health and maximizing the quality of time spent with all children in the home.

SCHOOL AGE

The school-age period is characterized by evolving cognitive skills and an increased emphasis on peer relationships. As children's cognitive and language skills expand, they are able to communicate better about their own beliefs and expectations related to their illness. This may facilitate effective psychoeducation that targets misinformation and addresses unfounded fears or concerns. It is essential that children's sense of ownership and control over their chronic illness be encouraged during this period in order to develop skills and self-efficacy related to self-management and collaboration throughout the lifespan. Unfortunately, the opportunity to develop child self-care skills appears to be missed frequently. Savage and colleagues(30) observed family-provider interactions during CF clinic visits, and found that most school-aged children were marginalized by staff, felt bored and perceived the interaction to be only between

their parent and the provider. In addition, children's own health priorities were not addressed. For example, diet consultations were focused toward the parent and emphasized weight gain, whereas children reported that their primary desired outcome for increased nutrition was more energy(30). Clearly, children will be more interested in adopting healthier behaviors if these behaviors are framed toward outcomes personally desired and meaningful to school-age children.

While cognitive changes can impact children's relationships with health providers, it is really peer relationships that are a core catalyst for the psychosocial development of the school-age child. Children's identity and sense of competence begin to be developed largely through a process of comparison with their peers(31). For the child with CF, this peer comparison process may highlight their CF-related differences (e.g., frequent coughing, taking enzymes with meals, more fatigue, school absences). Children who were diagnosed at birth or in early childhood may, in effect, undergo a second "diagnostic period" during which they realize at a deeper level the impact of CF on multiple aspects of their life. School-age children with CF describe significant concerns related "being different" than their peers, with a high premium on appearing "normal"(32). Coping with negative peer reactions such as teasing or overprotection in response to the visible manifestations of CF is reported to be one of the most stressful daily events for children with CF(32). Even with supportive peers, children seek to diminish the emphasis placed on their illness. Unfortunately, children are often unsuccessful at truly hiding the more "visible" aspects of the disease, and may in fact be setting themselves up for worse peer issues because providing the CF context for atypical behaviors may minimize negative peer perceptions(33). Keeping illness status a secret can also negatively impact the ability to develop and maintain intimate friendships(31–32).

Support from peers who share the same medical illness has often been promoted in order to circumvent the potential for stigmatization, decrease the sense of alienation and increase sharing of adaptive strategies to maintain quality of life. Prior to the mid-1990s, children with CF were encouraged to attend CF-related summer camps and other venues for peer support, and while empirical evidence is lacking, research with other chronic illnesses would suggest that these experiences were beneficial for increasing adjustment(34). However, in the mid-1980s CF medical communities became highly cognizant of *Burkholderia cepacia*, a particularly treatment-resistant constellation of bacteria that can be contracted from environmental sources and person-to-person transmission, and that often corresponds with rapid decline in lung functioning for patients with CF. It was soon determined that CF summer camps were the setting for epidemic spread of this bacteria, and these programs were closed (35). Other treatment-resistant bacteria have since been identified, and evidence of epidemic spread has been found within outpatient CF clinics as well as on inpatient hospital wards(35). In reaction, CF Centers have implemented strict segregation policies (e.g., isolating children with CF from each other during clinics) and have strongly recommended that patients with CF not interact with each other(36). There is little research looking at the emotional consequence of the stricter infection-control policies. However, some studies suggest that both parents and children are in agreement with the policies due to the health-benefits incurred by segregation, but also identify costs such as decreased social support, feeling alienated and missing friends with CF(37–38). Thus, children and adolescents with CF, while having similar challenges with healthy peers as do other children with chronic illnesses, are not afforded the benefits of support from those peers with CF who would most closely understand their experiences.

The additive psychosocial challenges incurred by CF during this age period appear to increase the risk of psychological distress in these children, although there is some disagreement in the literature(10,39). In a study utilizing semi-structured diagnostic interviews, 60% of children with CF met criteria for a psychological diagnosis, with an anxiety diagnosis present in 35%. Externalizing diagnoses were also present, with a prevalence of 22.5% for oppositional defiant

disorder and 12.5% for conduct disorder(40). Depression rates have been found to range from 2–9% in some studies to as high as 33% in more recent studies(39). Poorer adjustment in this age-group has been related to higher levels of stress, lower self-efficacy, increased monitoring for CF-related cues and less internal health locus of control(40–41). Other cognitive factors from the general chronic illness literature that may be relevant are illness uncertainty (the degree to which children experience confusion related to illness status and course)(42) and parental perception of child vulnerability(43). The life-limiting nature of CF, growth problems and significant respiratory symptomatology may render parents of children with CF particularly susceptible to viewing their child as "fragile". The communication of this perception (either overtly or subtly) coupled with the unpredictable course of CF may negatively impact children's developing self-concept because they may learn to perceive themselves as lacking the skills needed to manage disease-related factors.

Behavioral and cognitive-behavioral (CBT) interventions are generally considered to be first-line treatments for depression and anxiety in the general population of school aged children (44–45). There is a dearth of literature applying these evidence-based treatment protocols to enhance adjustment in the CF population. However, two recent studies did integrate cognitive-behavioral features such as problem-solving, anticipatory guidance, behavioral modeling and relaxation training into their interventions. In one study, children 8–12 years old with CF were randomly assigned to either a control group or to a "Building CF Life Skills" intervention which targeted problem-solving and social skills(46). The intervention was delivered in one home visit and one small-group intervention. Both loneliness and perceived impact of CF were improved relative to control at immediately post-intervention as well as at the 9 month follow-up. The use of a "group" intervention was particularly noteworthy in this study given the usual strategy of isolating children with CF from each other for infection-control purposes. Here, any children with drug-resistant infections were in separate clinic rooms connected by a real-time video camera link which gave the children a rather rare opportunity to form a "live" CF peer group(46). Another study utilized a CD-ROM program to increase CF-related knowledge and expand the coping repertoire of 10–17 year old children. Results showed that children randomly assigned to the CD-ROM condition evidenced greater disease-related knowledge and generated more coping strategies to hypothetical challenging situations when compared with a wait-list control(47).

In addition to challenges related to psychosocial functioning, health-related behaviors may become increasingly compromised as children grow older. Treatment burden is high during this period, with pre-teen children spending more than an hour/day completing treatment-related tasks(48). The time intensive nature of disease management may increasingly interfere with school and peer-related demands of childhood. A recent study used diary data assessment methods to document ACT adherence in school-aged children and found only 51% of the recommended ACT were completed, and of those completed, 64% lasted the recommended duration(49). In this same study, diary data indicted that adherence to both enzymes and nebulized medications were below 50%(49). Several barriers to adherence have been identified, such as lack of knowledge of CF in general and of individual treatment recommendations, disagreement with provider recommendations, complexity of treatment, psychological issues (on both the part of the parent and the child), "forgetting", oppositional behaviors, difficulty with time management, and child's low level of disease symptoms(50–52).

Research targeting improved adherence to CF treatment has demonstrated the short term benefits of behavioral interventions for school-aged children with CF. In a recent multi-site randomized clinical trial comparing a behavioral versus nutrition-only intervention, children in the behavioral treatment group had nearly double the daily caloric intake than did the children in the nutrition group after the 9 week treatment. Interestingly, between group differences

disappeared at the 2 year follow-up, at which point all the children maintained approximately 120% DRI. Analysis of the nutrition intervention suggests that this treatment included important behavioral components such as weekly monitoring of intake, successive approximation toward goals and individualized goal plans, suggesting that behavioral approaches, whether implemented in strictly "psychological" interventions or integrated into the work of other disciplines are successful at improving health behavior for school-aged children(53). Single-subject studies have documented the efficacy of behavioral interventions for increasing at-home exercise(54) and ACT(55–56). A randomized clinical trial investigating a self-administered education program based on the cognitive-behavioral and social learning models was shown to be effective in improving adherence to prescribed aerosol treatment in this age group, with an improvement in ACT only on the days that child was feeling unwell (57).

There are few studies examining the impact of CF on the family of the school-age child. However, a recent study of a clinic sample of parents of children in this age range revealed elevated rates of both anxiety and depression in both mothers and fathers, with rates of anxiety approaching 50%. Overall, however, parents reported a positive quality of life(58). Correlates of better parent adjustment have been shown to include less self-blame, less avoidant coping and more social support for parents, family cohesion and parental hope for positive outcomes for their children(12,59). These correlates appear to differ between mothers and fathers(59). As might be predicted, parents are particularly concerned with and impacted by their child's worsening disease status and possibility of death(58). Systematic interventions directly targeting the mental health of CF parents are sparse, despite the relationship between child and parental distress. However, one study examined the benefit of massage therapy for both school-age children with CF and their parents. Compared to a "reading together" only group, both child and parent anxiety were improved in the massage group, as was child peak air flow(60).

Clinical implications

The peer- and treatment-related challenges and evolving cognitive development that the school-age years bring to the child with CF offer a tremendous opportunity for children to develop or enhance critical psychosocial skills that are important for adjustment. For example, helping children develop effective means of handling awkward social situations related to their CF can expand their social behavior repertoire leading to greater confidence in navigating social situations. In addition, using behavioral methods to enhance adherence and track relevant outcomes can increase children's sense of involvement, control and self-efficacy, essential components of self-management across the life-span(61). As parent perception of their child's vulnerability may impact child self-perception, it is important to also work with parents to identify if these perceptions are present. Normalizing these reactions while also encouraging parents to have developmentally-appropriate expectations for behavior and allowing children the opportunity to learn from their mistakes will be important to keep child development on course. Finally, the cognitive growth during this period, in conjunction with evolving social skills, makes this an optimal time to fully engage children in collaboration with health care providers. Working with children to clarify what would be personally motivating in terms of physical or psychosocial outcomes and then realistically linking health behaviors to the child's own values will likely promote goal-driven behavior as well as help children make the connection between self-management and goal attainment in multiple arenas.

ADOLESCENCE

Adolescence is a period of rapid social, cognitive and physiological changes. The proportion of time spent with peers increases relative to family time, with peers also becoming more influential(31). Relatedly, adolescence is characterized by persistent movement toward increasing autonomy and separation from parents and adolescent-parent relationships are

frequently characterized by conflict(28). Cognition becomes more abstract and self-concept continues to be refined though experiences such as “trying on” different roles and behaviors which sometimes has negative health implications. Concomitant with puberty, sexual exploration adds another level of complexity to social relationships(28). At the same time as this tremendous developmental growth, CF typically worsens during adolescence, particularly for females, and the presence of more frequent symptoms (especially cough and fatigue) and pulmonary exacerbations (intense period of disease activity) correspond with greater illness burden(62).

Thus, the interface between biopsychosocial development and disease progression can make this time period particularly challenging for the adolescent with CF. When they would typically be gaining more independence, immersing themselves in peers and thinking about the future, their worsening disease may cause them to be isolated from peers due to the need to be home-bound or admitted to the hospital, to be more reliant on family and to have a heightened sense of a foreshortened future(63). This may be particularly salient for females who have been shown to have a higher mortality rate and poorer health-related quality of life than males(64). Declines in pulmonary function start earlier for girls, and the relative risk of survival for females compared to males is much lower up through the age of 20 years old. A number of factors are thought to be related to this gender difference, including girls reported tendencies to be less adherent to the high-fat diet and other aspects of treatment, to suppress coughing due to the greater public self-consciousness seen in females, to utilize passive coping more frequently, the normative reduction in physical activity noted for adolescent females, and higher levels of strain reported by females(65).

Research has examined the impact of CF on some developmental processes. For instance, Meijer and colleagues examined peer interactions in a chronically ill adolescent sample comprised of 98 adolescents (1/4 with CF). Compared with healthy norms, females with a chronic illness were significantly less socially engaged but as socially skilled. Females with CF were notable for higher levels of assertiveness. Males with a chronic illness displayed fewer problematic social behaviors with a trend toward being less socially engaged. Interestingly, duration of illness was *positively* associated with social skills and assertiveness, suggesting that one possible benefit of the chronic illness experience is developing a greater facility for negotiation. Perhaps the need to manage symptoms and interface with health care providers from a young age helps youth become more adept at identifying their needs and getting them met(66). Other studies have looked at the supportive behaviors of peers and families in adolescents with CF and suggest that families provide more tangible support and peers provide more emotional and companionship support. However, unsupportive family behaviors appear to be particularly problematic for adolescent adjustment(67). Interestingly, peer support may serve as a buffer for negative family interactions, whereas families do not appear to protect against the impact of strained peer relationships(68).

CF has also been examined in the area of teenage risky behaviors. For example, while chronically ill youth have been shown to have an increased rate of risky behaviors relative to healthy peers(69), youth with CF report fewer risky behaviors related to alcohol, tobacco and marijuana relative to healthy peers. However, 20% of youth with CF report having smoked, a concerning statistic given the impact smoking has on nutrition and pulmonary function(70). The prevalence of eating disorders, which typically begin in adolescence, is another risky health behavior with particular relevance to CF because of the relationship between nutritional status and mortality(71). A recent study utilizing rigorous diagnostic methods for eating disorders did not find an elevated prevalence of adolescents with CF meeting full criteria for an eating disorder relative to the general population. However, subclinical levels of eating disturbance were elevated compared to the general population, with 53% of the adolescents with CF indicating disturbed eating attitudes versus 40–47% of adolescents in the general population.

Of concern, 18.8% of the females and 7.1% of the males reported engaging in weight-loss behaviors despite the fact that the average BMI in the sample was just at the lower limit of the healthy weight range(71). Finally, while CF imposes a modest delay on puberty, sexual libido is not affected and some, but not all, research suggests that these youth have similar onset of sexual behaviors(70,72).

The limitations of CF not withstanding, the majority of adolescents report a high quality of life (6). Recent research has begun to investigate cognitive factors related to adjustment in this population, which may be particularly relevant during adolescence because of evolving cognitive development. One such variable is hopefulness. Szyndler and colleagues examined a number of variables related to quality of life and psychopathological distress in an adolescent CF sample and found that hopefulness was correlated with better physical, social and emotional functioning(6). One newer line of research in late adolescent and emerging adulthood development is the impact of chronic illness on goal pursuit, termed “health related hindrance” (HRH)(73). In a recent study of 18–28 year olds with chronic illness (divided between patients with CF and cancer), the more that the illness impeded goal pursuit, the more psychological distress and the less subjective well-being the individuals experienced(73).

Another variable that has been recently studied in adolescents with CF is the concept of acceptance. Acceptance reflects an individual’s ability to acknowledge and tolerate aversive thoughts and emotions even as they work toward achieving meaningful goals related to their values, and is a key component of the Acceptance and Commitment model of therapy(74). While the full model has not been researched in CF, Casier and colleagues explored the idea of acceptance in a sample of adolescents with CF found that adolescents who thought that they had the ability to live with CF and manage the associated negative consequences scored lower on measures of anxiety, depression and functional disability(75). Similarly, Abbott and colleagues also found that “optimistic acceptance” (i.e, accepting the CF diagnosis, using problem-focused coping and staying optimistic about the future) was related to better psychosocial quality of life in a sample of young adults, whereas distraction (i.e., attempting to forget about CF) was related to worse quality of life(76). Finally, despite the movement toward more autonomy from family, family variables such as organization, cohesion and emotional expressiveness has been shown to associated with better psychological functioning in adolescents(6).

Research on the level of psychopathology in adolescents with CF is conflicting. Whereas some studies have not shown a higher risk for psychological distress in this population(6), others have. For instance, in a recent study utilizing structured diagnostic interviews with children with CF ranging from 9 – 17 years of age, 57% met DSM criteria for at least 1 psychiatric disorder. Anxiety was the most prevalent disorder, with 30% of the youth with CF meeting criteria(52). A very low rate of depression was noted in this study, with only 2% of the youth meeting criteria. Higher rates of depression have been noted in other studies of adolescents with CF, although anxiety consistently appears to be the more prevalent of the two disorders (39). As seen in the child literature, CBT has been shown to be effective in the general population for both adolescent anxiety and depression(44,77). Interpersonal therapy (IPT) has also been successfully used with adolescent depression, and the combination of medication with CBT or IPT may be most effective for some adolescents(44). Given the importance of weight maintenance as well as the compromised function of multiple organs secondary to CF, the side effect of psychopharmacologic mediations must be carefully monitored. While between-group studies have not been conducted exploring the use of evidence-based psychological treatment to improve psychological functioning in the adolescent CF population, case studies suggest that CBT can be effective in improving adjustment in adolescents with CF(78).

Just as development may affect variables related to psychosocial outcomes, developmental processes are also related to changes in health behaviors important to management of CF. Research consistently demonstrates that CF-related adherence worsens once children become adolescents, with up to 50% doing less than their prescribed treatment and up to 30% not doing any treatment(79). Cognitive factors are influential in this arena as well. For example, adolescents who believed that their treatments were necessary and that CF was responsive to treatment had better adherence, with indications that these beliefs mediate the relationship between age and adherence(80). Family factors and psychological distress are also thought to influence treatment decisions and behaviors. Adherence has also been shown to be associated with self-reported family cohesion and flexibility as well as observation-based ratings of overall positive family interactions, especially for tasks that are more challenging and require more family resources(52,81). Interestingly, while some research suggests that psychopathology negatively impacts adherence, a recent study revealed that anxiety may actually improve adherence, perhaps reflecting a greater preoccupation with the illness(52).

The relationships between adherence and the shift to greater autonomy for CF-related tasks has been of great interest in recent years because adolescents with CF are no longer as sick as they were 30 years ago, and have the opportunity to reach older developmental milestones if they successfully manage their disease. Recent research in this area has shown that responsibility for self-management increases throughout development with periods of regression often found during illness exacerbations(82). A study using computerized phone diaries showed that parents gradually decreased their time involved in their child's CF-related activities from pre-adolescent through later adolescent years, although their involvement in other types of activities remained the same(83). In this study, more supervision, particularly by mothers, correlated with better adherence regardless of patient age(83).

Adolescent-focused outpatient adherence interventions are lacking in this population, but several approaches appear to be promising. One newer approach that has been shown to be effective in other pediatric behavioral health issues is motivational interviewing (MI)(84). MI targets enhancing motivation to engage in healthy behaviors rather than developing specific adherence-related skills. This approach takes an accepting attitude to patients' ambivalence to change and collaborates through goal clarification and increasing self-efficacy for those behaviors that the patient think are important. This may be particularly appealing to adolescents who are themselves in the process of refining self-concept and individuation. Another approach is internet-based health interventions incorporating psychoeducation, cognitive restructuring and problem-solving have also shown promise in enhancing the self management of adolescents with chronic illness. This may be very appealing for adolescents who have grown up with great facility with web-based applications. Finally, other innovative approaches using developmentally appropriate technology such as cell-phones are in development(85).

The transition to more autonomy in issues related to health care goes beyond adherence behaviors for adolescents with cystic fibrosis. Unlike their peers 30 years ago, many adolescents will "age out" of the pediatric setting and will be expected to move to adult providers. Research exploring transition to adult CF clinics has shown that although the median age of transfer to adult care is 19 years old, transition-related discussions are not typically initiated until 17 years of age. In addition, as of 2008, only ¼ of CF Centers offered transition-focused visits(86). As noted earlier, evidence suggests that school-aged children may not be optimally involved in patient-health care team collaboration(30); thus, youth may suddenly find themselves expected to take responsibility for their health interactions in adult CF clinics without having been adequately prepared. In addition, anticipating leaving home and/or going to university may raise concerns about access to health care(63). Earlier involvement in health care collaboration, addressing individual-specific concerns for the future, demonstrating

collaboration between pediatric and adult providers, and occasional pediatric follow-up during the year of transition have been shown to be effective.

Clinical implications

Given the precipitous decline in disease status often shown in adolescence, engaging adolescents in self-management is of primary concern. Unfortunately, while typical adolescent autonomy is developed in part by being allowed the chance to experiment and learn from mistakes, the "mistake" of not caring for one's health can be life-threatening with CF. Thus, for maximum health benefits, parents may need to stay involved in supervising their adolescent's health activities for longer than they might have expected, but will need to shift to strategies that are more collaborative. Behavioral strategies such as successive approximation (e.g., having the adolescent independently manage one small aspect of treatment) tied to natural consequences such as more freedom may help keep the transition developmentally appropriate but still closely monitored. In addition, the notion of acceptance may be particularly relevant to the adolescent with CF, for whom "escape" is clearly not an option due to daily treatment burdens and symptoms. Acceptance-based skills such as learning to do treatment recommendations even though they are aversive, or staying engaged with friends even when fatigued may help adolescents with CF continue to achieve important developmental tasks and meaningful goals as they move into adulthood.

SPECIFIC MEDICAL MILESTONES

CF complications

The onset of cystic fibrosis-related diabetes (CFRD) is a medical milestone, which typically occurs during late adolescence and affects 10–15% of adults with CF. CFRD is often precipitated by a worsening of CF symptoms and is associated with earlier mortality(87). The additional treatment burden brought on by a second chronic illness complicates an already involved treatment regimen and requires learning a new set of health management skills. Some research suggests that those who manage their CF well may already have in place self-management systems conducive to effective integration of the new treatment burden into their daily life(87). In addition, while the new CFRD diagnosis initially may be experienced as overwhelming, most people adjust to the new treatment issues. However, when the development of CFRD coincides with significant CF disease progression, this second diagnosis can provoke a sense of powerlessness and psychological distress(87).

Another particularly distressing consequence of CF is CF-related pain. In a recent study, at least one episode of pain in the previous month was reported for 59% of children ages 1 to 18 years old and 89% of adults with CF, with the duration of pain exceeding 6 months for 55% of the children and 73% of adults(3). Multiple pain locations were common. Pain was reported to significantly impact quality of life in 50% of the children and 70% of the adults. Approximately 2/3 of children and adults indicated that their medical treatment improved their pain. Procedural pain was also highly prevalent, with approximately 80% of both children and adults reporting at least one episode during the past month, with high rates found in patients with severe disease. Over ¼ of children reported pain during ACT(3). Pain from blood-sticks was also significant, with 90% of all patient reporting anticipatory fear. Pain medication did not sufficiently treat the pain in 1/3 of all individuals in this study(3), suggesting that other pain management strategies are indicated. Chest pain appears to be particularly distressing for children, and may have negative implications for their ability and willingness to complete airway clearance techniques, thus posing a health risk(88). CF-related pain has been shown to be related to both physical and emotional functioning, as well as overall quality of life(88). Non-pharmacological cognitive-behavioral interventions have been shown to be helpful for

both procedural pain(17) and chronic pain across the lifespan(89), and should be readily introduced to patients with pain.

Hospitalizations

The clinical course of CF is characterized by pulmonary exacerbations which frequently necessitate hospitalization for intensive ACT and IV antibiotic treatment. The impact of hospitalization on overall adjustment is not known, but has been thought to negatively impact quality of life. In one study, inpatients with CF reported significantly worse quality of life than did outpatients despite having similar lung functioning, suggesting that there may be factors other than objective health status that accounts for CF-related admission(62). Research has suggested that as many as 2/3 of frequently admitted chronically ill children have major psychosocial factors contributing to the admission, such as somatization of personal/family difficulties, lack of appropriate living situations and medical or psychological issues in the parent(90). Interestingly, a randomized clinical trial exploring the benefits of a brief written self-disclosure intervention for adolescents and adults with CF found that the intervention group evidenced fewer hospitalization days than did the control group, despite the fact that there were no between-group differences in psychological or physiological outcomes. Specific mechanism for this effect could not be identified by the study design. However, the authors postulate that the process of writing may have promoted more active engagement and coping with disease-related issues, thereby causing these young adults to rely less on health care providers for support(91).

Despite the disruption that hospitalizations pose, they appear to offer psychosocial benefits as well. Post-pulmonary exacerbation psychosocial quality of life was better for individuals with CF treated in the hospital versus those who were treated at home, suggesting that factors such as increased 24 hour support by inpatient health care providers, greater improvement in fatigue or respite for parents may have longer-term psychosocial profit(92). Inpatients with CF are, in effect, a “captive audience” for the 1–3 week typical admission duration, which provides an often unexploited opportunity to enhance coping and self-management. Cognitive-behavioral interventions can be used effectively with hospitalized patients to enhance stress management, coping with pain, sleep challenges and other health-related challenges, which patients can also apply at home(93). In addition, CF-specific health behaviors can be enhanced by incorporating psychoeducation and evidence-based behavioral strategies into routine inpatient treatment. For example, our institution recently used quality improvement strategies to promote best-practice ACT on our adolescent unit. Evidence-based best-practice protocols were developed for a variety of ACT modalities, then patients were educated on proper technique per protocol and collaborated with their respiratory therapist to identify the ACT modality that was the best fit for them. Finally, behavioral strategies were implemented by unit staff which focused on positive reinforcement for ACT behaviors that met best-practice criteria. This program has resulted in significant increases in both the quantity and quality of the ACT that patients participated in(94). Generalization of optimal utilization of ACT from hospital to the home setting needs to be studied. Thus, the inpatient admission may be an opportunity for more in-depth assessment and intervention for important psychosocial and health-behavior issues.

End-stage lung disease (ESLD)

The current median age of death from CF is approximately 25 years old and the majority die from ESLD(1). Lung transplantation is the most aggressive treatment available for advanced lung disease, and is considered when predicted survival with transplant surpasses predicted survival with out. Approximately 120 – 150 with CF receive a transplant per year(95), and higher quality of life post-transplant has been reported(96). Five year survival rate is 50–60% for patients with CF who receive a transplant(95) and estimates suggest that up to 25% of

patients with CF will die while on the waiting list(96). Thus, even with the prospect of lung transplant, many teenagers and young adults will be faced with confronting end-of-life issues.

There is very little research on psychosocial aspects related to end-of-life in the CF population. However, there is some evidence to suggest that having survived multiple pulmonary exacerbations throughout the course of the illness, patients with CF in ESLD may perceive CF to be “beatable”(97), and the possibility of lung transplantation may contribute to this perspective(98). In addition, the chronic and progressive course of CF sometimes makes it challenging to know when it is the “right time” to have end-of-life discussions, but they are sometimes timed with transition to adult care providers or at annual review meetings with CF providers, which is preferable than during periods of disease acuity(97–98). There is typically a very short time period between institution of a do-not-resuscitate order and time of death (e.g., 5 days), suggesting that patients with CF continue with life-preserving measures within hours of death(98). Instituting palliative care treatment plans in conjunction with lung transplantation treatment plans may afford patients with CF the maximum comfort even as they await transplantation and at time of death(98). Honest communication maximizing provision of care options and emotional support, family involvement, attending to spiritual and psychosocial needs of patients and comprehensive symptom management are the cornerstones of end-of life care(99). Once a death has occurred, follow-up support to the bereaved family is also indicated, including referral for counseling for instances of complicated grief(99).

SUMMARY

Certainly, CF may complicate some of the processes inherent in psychosocial development, and there is much more research to be done clarifying the interface between developmental processes, psychosocial variables and health for the child with CF. The increasing focus on self-management and adherence from a developmental perspective can have a significant impact on meaningful health outcomes in this population. There is also exciting newer research focusing on positive correlates of psychosocial adjustment, such as hopefulness, acceptance and the importance of achieving meaningful goals despite CF. These variables relate to the concept of “positive psychology”, which is the field of psychology that explores the adaptive, more affirmative experiences of the human experience(100). While positive psychology has been under-studied in the field of pediatric psychology, it may be particularly relevant to understanding why many children and adolescents with CF report high quality of life despite the treatment burden of their illness. In addition, understanding if youth with CF undergo “post-traumatic growth” (i.e., experience meaningful benefits from their CF-related experiences) may point the field toward a clearer understanding of the full scope of the psychosocial experience related to this illness and may help elucidate the processes that promote living a full, meaningful and productive life within the context of a life-limiting illness(100).

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