

**NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES
WORKSHOP ON NON-ADHERENCE IN ADOLESCENTS WITH CHRONIC ILLNESS**

DoubleTree Hotel and Executive Meeting Center
Bethesda, MD
September 22 - 23, 2008

SUMMARY REPORT

Monday, September 22, 2008

WELCOME

Marva Moxey-Mims, M.D., Director, Pediatric Nephrology and Renal Centers Programs, Division of Kidney, Urologic, and Hematologic Diseases, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), Bethesda, MD

Dr. Moxey-Mims welcomed the participants, highlighted the importance of the topic to be discussed, and expressed hope that the meeting would provide valuable insight. She then introduced Dr. Rodgers.

OPENING REMARKS

Griffin Rodgers, M.D., Director, NIDDK, NIH, Bethesda, MD

Dr. Rodgers added his welcome, noting that over the next 2 days, the participants would hear what is known about non-adherence in adolescents and what is prime to understand. Studies show that medication non-adherence is associated with poor outcomes and that adolescents, in particular, have difficulty adhering to medical regimens. The purpose of this workshop is to identify, characterize, and understand risk factors associated with non-adherence in adolescents and to identify potential areas for future clinical studies.

INTRODUCTION AND CONFERENCE GOALS

Bradley Warady, M.D., Section Chief, Nephrology, and Director of Dialysis and Transplantation, Children's Mercy Hospitals and Clinics, Kansas City, MO

Dr. Warady presented data showing that graft survival of kidney transplants in adolescents is comparable to that in older and younger patients at 1 year but substantially lower at 5 years, a pattern that may be at least partly due to non-adherence. Findings like these have prompted a focus on adolescents in non-adherence research. The goals of this conference are to:

1. Review the literature on non-adherence in adolescents with chronic illness;
2. Share and discuss experiences and opinions; and
3. Generate ideas for future studies.

The key product of the conference will be the workgroup reports on research needs and priorities, for potential incorporation into future NIDDK initiatives.

BACKGROUND

Moderator: Dr. Warady

Definition and Heterogeneity of Non-adherence

Terence F. Blaschke, M.D., Professor of Medicine and Molecular Pharmacology, Stanford University, Stanford, CA

Dr. Blaschke began by noting that the problem of medication non-adherence has been recognized since the time of Hippocrates. Today, it is sometimes referred to as “America’s other drug problem.” Three elements of a dosing history determine drug actions and efficacy: (1) the size of doses; (2) the time intervals between doses; and (3) the duration of treatment. Satisfactory adherence is achieved when the gaps between a patient’s dosing history and the prescribed dosing regimen have no effect on therapeutic outcome.

The measurable components of adherence are:

- Acceptance (Will the patient even begin the therapy?)
- Execution (How well does the patient carry out the recommended regimen?)
- Persistence/discontinuation (Does the patient continue or abandon the regimen?)

Adherence is better in acute than chronic illnesses. In chronic conditions, persistence is a major problem, and the severity of disease does not correlate with better adherence. Typical execution/persistence rates are 50 to 60 percent, with 40 to 60 percent of patients abandoning medications by 1 year. Persistence is better for diabetes, with 75 percent taking medications after 1 year. Adherence research and interventions must take into account both the consequences of and reasons for non-adherence. Reliable methods of measurement and analysis are needed for both.

Methods of measurement include asking the patient, interviews/questionnaires, physician/nurse assessment, database reviews, drug assays (blood or urine), assays for marker compounds, and the use of electronic monitoring devices. The former methods generally provide qualitative adherence data, not a detailed dosing history. Electronic monitoring provides the precise and rich information that is required for individualizing interventions, but patients may confound the interpretation of these data if medication bottle openings (what the device actually measures) do not correspond to drug ingestion (e.g., if the patient removes extra doses for later use or takes an incorrect number of tablets).

Dr. Blaschke concluded by noting that variable adherence to prescribed therapy should be accepted as a given. Researchers and clinicians need to utilize good measures of adherence so that they can determine how much adherence is sufficient and so that they can find ways to address individual patients’ adherence problems.

Discussion

Dr. Eyal Shemesh observed that some patients find that monitors do not fit with their usual dosing aids and that recruiting those who are least adherent can be difficult. Thus, studies involving monitors may focus on the wrong patients. Dr. Blaschke agreed that the use of

monitoring devices could create selection bias but noted that the currently available data come primarily from clinical trials, and the participants in such trials are not representative of the overall patient population, who may be even less adherent. Dr. Philip Zeitler asked whether people who persist longer tend to be more adherent. Dr. Blaschke responded that there is actually a slight decline over time in percentage of doses taken as therapy continues, and that two patterns of discontinuation occur among those who stop taking a drug: one-half stop suddenly, but the others develop a pattern of taking it irregularly before discontinuing. Irregular drug use is a signal that discontinuation is imminent. Dr. Keith Slifer asked how data are transferred to the iAdherence website illustrated in Dr. Blaschke's slides (<http://www.iadherence.org/mainPage.action?maintab=0>). Dr. Blaschke responded that the data are downloaded from the monitoring device; nothing is done by hand. A centralized database is generally used in clinical trials, but a practicing clinician would need only the device, a reader, and a computer; access to a central data repository is not necessary.

The Medical and Economic Impact of Treatment Non-adherence in the Adolescent

Fabienne Dobbels, Ph.D., Postdoctoral Fellow, Centre for Health Services and Nursing Research, Katholieke Universiteit Leuven, Leuven, Belgium

Dr. Dobbels reported that approximately 15 percent of adolescents have chronic illnesses and thus face the challenges of illness in addition to those of growing up. Poor adherence in adolescents with chronic conditions may be related to their poorly developed abstract thinking and planning, difficulty in imagining the future, tendency toward risk-taking, and rejection of the authority of medical professionals as part of the process of separation from parents.

Although the use of medication has been the focus of most adherence studies, medical regimens may include a variety of other behaviors, including appointment-keeping, screening, healthy behavior, exercise, and diet. A previous meta-analysis of studies on adherence to each of these aspects of treatment regimens showed an average of 25 percent non-adherence, with better adherence in adults than pediatric patients and better adherence to medication than to other components of medical regimens. Better outcomes have been observed in adherent patients, but prior analyses of outcome research have not focused on adolescents.

Dr. Dobbels and her colleagues have conducted a new meta-analysis of 22 studies of adherence in adolescents, all of which measured clinical outcomes and used precise definitions of adherence; four studies on diabetes were included. Preliminary results indicate that the likelihood of a good outcome is 32 percent higher in adherent than non-adherent adolescents. The meta-analysis has some methodological limitations, however. The definitions of adolescence, definitions of adherence, and methods of measuring adherence varied among studies, and some studies lacked prospective designs or did not clearly define clinically relevant outcomes. Dr. Dobbels also noted that because non-adherent patients often refuse to participate in adherence studies, the meta-analysis may actually have underestimated the true impact of non-adherence on outcome.

Non-adherence may lead to both direct economic consequences (such as the cost of avoidable hospitalizations) and indirect ones (such as missed school/work days). No studies have specifically examined the economic cost of non-adherence in the adolescent population. In some

instances, adherence may actually be more costly than non-adherence (e.g., because adherent patients may live longer and therefore use more medical resources). Thus, consideration of both costs and outcomes through cost-benefit analysis, cost-effectiveness analysis, or cost-utility analysis is necessary.

Multiple Risk and Adolescent Adherence: A Developmental Contextual Framework

Barbara H. Fiese, Ph.D., Professor and Director, Family Resiliency Center, University of Illinois at Urbana-Champaign, Urbana, IL

Dr. Fiese began her presentation by pointing out that risk rarely occurs in isolation. Clusters of risk factors for a given negative outcome are commonly present, and no single factor accounts for the bulk of variance. As the number of risk factors increases, a steep drop-off in positive outcomes often results, frequently as a quadratic rather than linear function of cumulative risk.

The concept of multiple risk can be applied to non-adherence in adolescents. In risk research, it is important to focus on factors that are amenable to change and on resiliency and protective processes in the face of daily challenges.

Relevant risk factors for adolescent adherence/non-adherence include gender, age, and disease status (severity, time since diagnosis, and disease course), as well as a variety of family factors, including family structure (the number and education level of adults in the household, economic resources); family management (routines, teamwork, organization); and family climate (emotional investment in the treatment regimen, disease burden, cohesion, conflict).

Cultural ecological factors may also influence adherence. For example, neighborhoods may provide easy or difficult access to healthy foods and safe environments for exercise. Transportation issues may influence access to health care and the ease or difficulty of filling prescriptions. Acculturative stress (immigration, language barriers), perceived discrimination, and health beliefs related to trust in medical regimens all may influence adherence.

Several methodological issues are important in the design of studies involving multiple risk factors. Information should be collected on at least four and preferably six to eight risk indicators. The dichotomous nature of most of the commonly used risk indicators is a cause for concern; categorizing an indicator as merely “high” or “low” leads to a loss of potentially important information. It is important to test for curvilinear and well as linear effects and to maintain a methodological strategy of assessing the cumulative effect of risk factors rather than attempting to determine which factors contribute the most. Adherence to different parts of a treatment regimen, such as diet, medication, and exercise, should be assessed separately because their relationships to cumulative risk may differ.

Discussion

A participant asked how one could go from broad-scale investigations of multiple risk factors to the planning of interventions. Dr. Fiese indicated that risk stratification or a tailored intervention model could be useful. Although it may not be possible to address all of the risk variables, it can be valuable to tailor interventions to specific family ecology variables and stressors.

Dr. Warady asked how successfully health care providers detect risk factors for non-adherence. Dr. Fiese responded that this would be a wonderful topic for a study; it speaks to the importance of continuity of care and of the need for providers to ask what else is going on in a family's life.

Measuring Adherence to Medical Regimens

Suzanne Bennett Johnson, Ph.D., Professor of Medical Humanities and Psychology, Florida State University College of Medicine, Tallahassee, FL

Dr. Johnson began her presentation by noting that adherence is often defined as the extent to which a person's behavior coincides with health or medical advice. Health advice, however, is an illusive standard. It is important to ask whether the advice is communicated effectively to the patient, whether it is documented, whether it is consistent with current standards of care, and whether, if followed, it would actually make a difference in the patient's health status.

Often, health care providers make more recommendations than patients recall, and patients may recall some advice incorrectly. Providers may not document recommendations other than medication. In addition, providers often fail to meet standards of care (e.g., in one study only 58 percent and 17 percent, respectively, adhered to the standards of an annual cholesterol exam and an annual dilated eye exam for patients with type 2 diabetes).

Providers fail to follow practice guidelines for a variety of reasons: lack of awareness of the guideline or its specific recommendation, disagreeing with the guideline, forgetting to implement the guideline, and lack of time during patient visits. Even if recommendations are implemented, they may not be helpful. One recent study showed no significant relationship between medication adherence and blood pressure in patients with hypertension, and another showed no effect of blood glucose (BG) monitoring on hemoglobin A1c (HbA1c) values in newly diagnosed patients with type 2 diabetes.

Patients' knowledge and skill deficits may lead to inadvertent non-adherence. Studies have shown, for example, that more than one-third of patients make clinically significant errors in the use of insulin. The problem of inadequate knowledge and skill often receives insufficient attention in adherence research. Patients often believe they are following the provider's recommendation, but because of knowledge or skill deficits they are inadvertently non-adherent.

Several conceptual issues in the measurement of adherence need to be considered. Should adherence be considered continuous or dichotomous? Univariate or multivariate? Static or dynamic? Worth measuring in its own right or only in relationship to a standard? Dichotomous measures probably are justified only when the minimum behavior necessary to achieve a clinical effect is known—a rare situation. A multivariate approach is preferable to a univariate one because adherence to one component of a medical regimen does not predict adherence to other components of the regimen. Adherence is primarily dynamic over time; for example, it may improve just prior to a clinic visit. Consequently, a dynamic measure of adherence is usually preferred over a static one. If a standard is used, careful consideration must be given to its selection and measurement.

Adherence may be measured by direct observation (a difficult and time-consuming method but useful for detecting skill deficits), blood or urine assays, pharmacy records, self-report, 24-hour recall interviews or daily phone diaries, or electronic monitors. Dr. Johnson recommends against the use of health status or provider ratings because they are influenced by factors other than adherence. Self-report can be effective if methods that provide permission to acknowledge non-adherence are used. Electronic monitoring is continuous and dynamic but is available only for some behaviors and may be costly and technically difficult.

Discussion

Dr. Richard Fine commented that in the adolescent transplant literature, failure is often attributed to non-adherence but researchers do not explain how they determined that the patient was non-adherent. Dr. Johnson agreed that this was a problem, noting that the use of physician ratings is circular because it involves the assumption of a link between adherence and health outcomes. Dr. Tej Mattoo asked about the role of parents in assessing adherence. Dr. Johnson said that substantial data exist on the role of parents. Parent measures of children's adherence are most accurate when a child is young but become less useful as children grow older. For adolescents, parents often are unaware of the adolescent's behaviors and sometimes report better adherence than the adolescents themselves do.

SCOPE OF THE PROBLEM: A DISEASE-SPECIFIC PERSPECTIVE

Moderator: Lori Laffel, M.D., M.P.H., Chief, Pediatric, Adolescent, and Young Adult Section, Joslin Diabetes Center, Boston, MA

Teens, Pre-teens, and Type 1 Diabetes

Tim Wysocki, Ph.D., A.B.P.P., Clinical Psychologist, Division of Pediatric Behavioral Health, Nemours Children's Clinic, Jacksonville, FL

Dr. Wysocki began his presentation by observing that the complexity of regimen adherence for adolescents with type 1 diabetes is awesome. Thus, a simple adherent versus non-adherent dichotomy is not appropriate. Variables associated with differences in adherence include parent-adolescent conflict, single-parent family structure, deficient parent-adolescent communication, premature withdrawal of parental involvement, absence of clear expectations for self-care, a coercive family process, the psychological adjustment of the parents and youth, and parents' diabetes problem-solving skills. Unfortunately, information on adherence is not yet being used effectively to guide clinicians.

Research results indicate that caregivers' diabetes problem-solving skills are good predictors of HbA1c levels, but youths' skills are not; this may reflect youths' unwillingness to engage in diabetes self-management behaviors in the presence of peers.

The role of parental involvement is illustrated by research in which youths rated the involvement of their primary and secondary caregivers in diabetes management. When both caregivers were rated "low," adherence and HbA1c were poorer than when both were rated "high."

Research in behavioral psychology has established that: (1) behavior is much more strongly controlled by immediate than delayed consequences; (2) behavior that is reinforced intermittently is stronger than behavior that is reinforced consistently; (3) avoidance of aversive events may encourage “superstitious” behaviors; and (4) unsuccessful avoidance of adverse events may lead to “learned helplessness.” Diabetes self-management behavior in adolescence has both positive and aversive consequences. It leads to better health and quality of life, lifestyle flexibility, avoidance of complications, and positive responses from adults, but at the same time, it causes pain, takes time and effort, and may lead to criticism, social stigma, conflict, and loss of privacy. In diabetes self-care, consequences are often delayed and loosely related to a specific self-management act, and adverse events may appear capricious. For example, infrequent BG checks usually yield no discernible diabetes-related immediate negative consequence, and they lessen pain, inconvenience, bad news, and conflict with parents over out-of-range results. Thus, adolescents may be motivated to skip BG checks.

Fear of hypoglycemia may motivate adolescents and their families to keep BG higher than the medical team would prefer. Thus, in addition to other motivators, unscheduled snacking and skipping or delaying insulin may seem desirable to an adolescent with diabetes because these behaviors reduce the risk of hypoglycemia.

Several empirically validated interventions to improve diabetes self-management have been developed. Commonalities among them include: theoretical grounding; a focus on diabetes-specific target behaviors; the use of experiential learning; a flexible, individualized approach; sensitivity to cultural diversity; and a sustainable delivery system.

Discussion

A participant asked whether anything can be learned from adolescents and families who adhere well to diabetes self-management regimens. Dr. Wysocki said that many families do very well. Families who regard out-of-range BG values as an opportunity to teach and problem-solve rather than reacting with shame and blame are likely to have better adherence. Also, adolescents who develop a view of diabetes as something they can contend with rather than something that they despise are more likely to emerge from adolescence with good self-management practices.

Type 2 Diabetes and Prediabetes in Youth

Philip Zeitler, M.D., Ph.D., Professor of Pediatrics, University of Colorado at Denver, Aurora, CO

Type 2 diabetes is different from the other chronic illnesses under the NIDDK research mission, Dr. Zeitler stated, because family structure is often the *cause* of the illness; unlike type 1 diabetes or many digestive or kidney disorders, type 2 diabetes does not strike capriciously.

Type 2 diabetes occurs in a complex psychosocial setting. Adolescents with type 2 diabetes are predominantly from minority groups (African American, American Indian, or Hispanic), are predominantly female, are obese, and usually come from families in which first-degree relatives have type 2 diabetes; thus, the family faces heavy health burdens even before the young person’s diagnosis. The parents with diabetes generally have poor diabetic control, and multiple family

members, both with and without diabetes, are obese. In families with type 2 diabetes, diets tend to be high in fat and low in fiber, with frequent binge eating, no routine exercise, lengthy periods of television watching, and a high prevalence of insulin resistance among non-diabetic family members. Family dysfunction, as reflected by unstable residence, contact with the justice system, poor school attendance, poor parenting, and domestic violence, is prevalent.

The care requirements for adolescents with type 2 diabetes are substantial, involving clinic visits every 3 months, glucose monitoring two to four times a day with logging, the use of medications several times a day, and dietary and activity changes. Relatively few hard data on adherence to these requirements exist, but the limited data available indicate that adherence is often poor. NIDDK is currently supporting a randomized controlled trial called 2TODAY (for Treatment Options for type 2 Diabetes in Adolescents and Youth) that is comparing three treatment regimens for type 2 diabetes. The trial includes a highly structured adherence support program, and only those who are adherent during the run-in period are accepted into the trial. In general, adherence to medication and bringing meters to clinic visits has been good in the early stages of the trial, but adherence has decreased over time.

HbA1c values in non-white patients with type 2 diabetes are poorer than those in white patients. This difference may reflect disparities in self-management behavior (less family support, poorer financial resources, or limited access to programs and healthful food). Biology may also play a role; worse insulin resistance has been observed among minority youth.

Discussion

A participant asked whether any pharmacokinetic studies had been conducted at different ages to look for biologic differences in response due to puberty. Dr. Zeitler replied that no such studies had been reported.

The Adolescent and Kidney Transplantation: Where Does Medication Non-adherence Fit In?

Robert Ettenger, M.D., Chief, Pediatric Nephrology, Department of Pediatrics, University of California at Los Angeles, Los Angeles, CA

Eileen Tsai, M.D., Assistant Professor, Mattel Children's Hospital at the University of California at Los Angeles, presented this talk on behalf of Dr. Ettenger.

Adolescence is a time of emerging autonomy and multiple crises, many of which may be undetected. It is also a time when the risk of kidney transplant failure is high. Non-adherence is believed to play a role in graft failure, but heightened immune responsiveness, combined with increased viral exposure during adolescence, may also contribute.

Data from Mattel Children's Hospital indicate that non-adherence to medication in kidney transplant patients is much higher among adolescents than pre-pubertal patients (3 or more days of missed medication: 53 percent among adolescents, 17 percent among pre-pubertal by direct report). Factors associated with non-adherence include female gender, family instability, insufficient social and emotional support, single-parent family status, low socioeconomic status,

low self-esteem, poor intrafamily communication, deficient acceptance of the end-stage renal disease (ESRD) diagnosis, and poor communication and socialization skills. Many adolescent patients have some or all of these characteristics simultaneously.

Non-adherence may reflect the various developmental stages during adolescence. Interventions that are appropriate at one age may become inappropriate as the young person gets older, so non-adherence may reflect the medical team's lack of attention to developmental changes.

It is important to remember that ESRD patients tend to be psychosocially younger than their chronological age. Behavioral and multi-component interventions have been shown to be relatively effective in promoting adherence in young people with chronic illnesses. A multi-level approach to non-adherence, targeting both the patient and medical team, seems most effective, and an individualized approach to non-adherence is likely to be more successful than a standardized approach.

Non-adherence in renal transplant patients increases after the transition from pediatric care to the adult care system, and transplant failures occur more often in transitional patients than in pediatric or adult transplant recipients. Transition to adult care should be based on developmental guidelines rather than arbitrarily on age. Assessment methodologies and toolkits for transition are needed, and formal adolescent transition programs would be helpful.

They Are What They Eat

Elizabeth J. Mayer-Davis, Ph.D., Professor, Department of Nutrition, University of North Carolina at Chapel Hill, Chapel Hill, NC

Dr. Mayer-Davis began her presentation by noting that adolescents with chronic diseases live in the same world that all young people do. Remarkably few data exist on the diets of adolescents with chronic disease. Most knowledge of this subject is extrapolated from studies of healthy adolescents or chronically ill adults.

The basic premise of dietary recommendations for adolescents with chronic disease is that dietary intake should promote normal growth and development while accommodating special disease- and treatment-related needs. The 2005 Dietary Guidelines for Americans emphasize weight management and choosing high-nutrient-density foods and also call for: (1) substantial physical activity; (2) consumption of fruits, vegetables, whole grains, and fat-free or low-fat milk or milk products; and (3) nutrient targets related to fat, saturated fat, cholesterol, and *trans* fats.

In addition to supporting normal growth and development, dietary recommendations for youth with diabetes should optimize glycemic control and minimize risks of dyslipidemia and related complications. Despite the absence of strong evidence for many aspects of diabetes dietary management, adherence to dietary recommendations has been associated with clinically meaningful decreases in HbA1c. Dietary counseling should be individualized and should consider: the insulin regimen; weight status; key metabolic targets; family, social, and cultural context; and taste preferences and psychosocial needs of the adolescent. In the SEARCH study, a multicenter project funded by the Centers for Disease Control and Prevention and NIDDK,

most youth with diabetes did not meet dietary guidelines, especially those for saturated fat, fiber, and grains, for which less than 10 percent met the recommendations.

Dietary recommendations for patients with celiac disease emphasize a gluten-free diet, sometimes with additional restrictions prompted by coexisting lactose intolerance. Folate supplementation is controversial. The dietary recommendations are less complex than those for diabetes but nevertheless difficult to follow because gluten is highly prevalent in the food supply. Compliance with a gluten-free diet is high in young children because of the role of parents and negative feedback from symptoms, but it drops off in adolescents, who may be willing to tolerate symptoms so that they can eat with their peers.

No studies have reported on the usual dietary intake or dietary adherence of adolescents with chronic kidney disease (CKD). Recommendations differ at different stages of CKD: phosphorus restriction and supplemental enteral feedings may be necessary prior to dialysis; increased protein, restricted phosphorus, and frequent feedings and/or supplements may be needed with peritoneal dialysis; and sodium, potassium, fluid, and phosphorus restrictions may be needed during hemodialysis.

UNDERSTANDING THE ADOLESCENT WITH CHRONIC ILLNESS

Moderator: Tom Nevins, M.D., Professor, Department of Pediatrics, University of Minnesota Medical School, Minneapolis, MN

Neurodevelopment in Adolescence and Its Impact on Treatment Non-adherence, Including Transition Issues

Maria E. Ferris, M.D., Ph.D., M.P.H., Associate Professor of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC

Dr. Ferris began her presentation by describing the cognitive changes that occur during adolescence, including increased capacity for the following: abstraction and advanced reasoning, impulse control, assessment of risk versus reward, use and manipulation of working memory, language use and skills, and self-regulation in emotional states. The human brain continues to develop and mature until the mid-20s, and thus patients who are legally adults may not be fully mature from a cognitive standpoint.

Chronic diseases are linked to cognitive and memory difficulties in both adults and children. In pediatric patients with CKD, longer duration and greater severity of illness have been associated with poorer memory and lower IQ, and depressed activation in the parietal lobe and prefrontal regions of the brain has been observed. At the University of North Carolina Kidney Center (UNCKC), adolescent/young adult patients take an average of nine oral medications per day, in addition to injectable medications, and their medication regimens are frequently changed at office visits. It is easy to see how cognitive difficulties might contribute to non-adherence to such complex treatment regimens.

The burden of disease treatment may also contribute to non-adherence. For example, pediatric patients treated at the UNCKC must travel an average of 75 miles one-way to see their doctors.

Transitioning from pediatric care to internal medicine care can be difficult. In a group of adults with pediatric-onset CKD, 45 percent currently miss medications and 40 percent had difficult transitions. Internists who care for transitioned patients may not be well prepared to meet their needs because these patients represent only a small proportion of the patients in their practices (less than 2 percent in one survey). Providers who care for transitioned CKD patients report that fewer than one-half know their medications and disease well and that the *parents* of these adult patients, rather than the patients themselves, are the ones who ask questions.

The University of North Carolina (UNC) has developed the UNC TR_xANSITION Program, an interdisciplinary program designed to teach, measure, and enhance disease self-management skills in adolescents and young adults with chronic conditions. The tools developed include a transition score, a transition-readiness survey, and a “medical passport” (a document that patients carry that gives details about their condition and medications). Among CKD patients in this program, overall transition scores are low (6/10), but retention of the passport is high (at 9 months, 78 percent still have it). An online game to teach CKD patients self-management skills and provide an opportunity to communicate with other patients is in development.

Discussion

A participant asked whether the UNC TR_xANSITION Program uses transition scores to determine when patients should be transferred to adult care. Dr. Ferris said that the score is primarily a diagnostic tool for now and has been used in transition planning for only a handful of patients.

Non-adherence: Psychosocial Correlates (Where Do We Go Next?)

Eyal Shemesh, M.D., Director, Behavioral Health Integrated Program, The Children’s Hospital of Philadelphia, Philadelphia, PA

Dr. Shemesh stated that it is assumed that psychosocial risks contribute to non-adherence and that minimizing those risks will improve adherence. Very few clinical programs, however, routinely assess non-adherence, assess risks associated with it, and clinically intervene to improve adherence when a risk is identified. These actions are not performed because of inadequate time, funds, reimbursement, and attention. In addition, scientists may not be using the correct methods in their research or evaluating the approaches most likely to lead to clinical success.

Dr. Shemesh contends that meta-analyses of observational studies should not be used to summarize results in this field because the known weaknesses of meta-analyses of observational studies are compounded by uncertainties specific to non-adherence. Also, researchers working on non-adherence often assess too many predictive variables, fail to distinguish between association and causality, do not define adherence in a consistent way, and use methodologies that promote selection bias. Patients who are most likely to complete the paperwork involved in adherence studies are also most likely to be adherent; thus, participants in adherence research tend to be those who do not have an adherence problem.

To improve the quality of adherence research, Dr. Shemesh recommends that:

- Studies of psychosocial predictors should have a defined threshold of adherence;
- Studies should be targeted, prospective, and use a singular conceptual framework;
- To minimize selection bias, the smallest possible numbers of questionnaires and variables should be used;
- Studies should deviate as little as possible from usual clinical practice; and
- Intervention studies should use feasible interventions and specifically target either non-adherent patients (with a clear definition of non-adherence as an entry criterion) or patients with a specific risk factor (with clear definitions of both the risk factor and non-adherence as entry criteria).

The only alternative to this approach, Dr. Shemesh stated, is to conduct very large studies with high statistical power.

Discussion

A participant asked whether there are as many problems in investigating the relationship between adherence and clinical outcomes as in the prediction of adherence. Dr. Shemesh replied that research on this topic also has issues but that researchers could easily improve methodology. In studies assessing the relationship between adherence and outcomes, distinguishing between association and causality is important. Well-designed, targeted studies are needed, and longitudinal research may be useful.

Competing Challenges and Family Issues

Barbara J. Anderson, Ph.D., Professor of Pediatrics, Baylor College of Medicine, Houston, TX

Dr. Anderson began her presentation with a quotation from Dr. Michael Rapoff of the University of Kansas, which states that non-adherence in the adolescent “may be part of a mosaic of patient and family struggles. Medical adherence problems may be symptomatic of or exist concurrently with patient and/or family dysfunction.”

Many traditional models for adherence or behavior change, including Social Cognitive Theory, the Theory of Planned Behavior, and the Health Belief Model, are based on assumptions that patients have single or limited risk factors, but in reality multiple and intergenerational risk factors are often present. A conceptual model developed by Dr. Paul Newacheck and colleagues at the University of California at San Francisco may be most useful in understanding this situation. The Newacheck model refers to five key domains of health—genetic endowment, physical environment, social environment, health-related behaviors, and the health care system—which are conceptualized as acting at four levels: the societal level, the community level, the family level, and the level of the child. This model addresses the interconnection between different layers of influence and can help researchers and clinicians identify how they can intervene to improve adherence.

Another valuable model is the Behavioral Model for Vulnerable Populations, which helps to elucidate the role of fatalism (learned helplessness) as a characteristic of vulnerable populations

with multiple risk factors and as a reason why traditional models for understanding adherence behavior may not apply to these populations. This model proposes that the use of health services and adherence to medical regimens are a function of: (1) a predisposition by people to adhere; (2) factors that enable or impede adherence; and (3) perceived health. Members of vulnerable populations often have competing needs (such as parents with multiple, unstable jobs; caregiving responsibilities for extended family members; and chronic conditions in other family members), chronic stressors, and limited personal and family resources. These factors prompt them to believe that events are out of their control and to view health and health risk factors from a short-term rather than long-term perspective. The Behavioral Model for Vulnerable Populations may guide researchers in maintaining realistic expectations for adherence and in identifying potentially modifiable factors that influence adherence. For example, when communicating with vulnerable families, health care providers may find it helpful to focus on relatively short-term adverse consequences of non-adherence rather than consequences that may not occur for decades.

Discussion

A participant raised the issue of providing supports to vulnerable families to reduce the competing needs problem, asking who is responsible for this and what kind of support should be provided. Dr. Anderson responded that too many people stand in judgment of parents from vulnerable populations. It is not that these parents do not care about their children's health; they do care. Rather, the problem is that their many other needs draw their attention away from their child's treatment regimen.

BREAKOUT SESSIONS: IDEAS FOR RESEARCH INITIATIVES

The Role of the Family in Adolescent Treatment Non-adherence

Chair: Dr. Wysocki

The Influence of Ethnic and Cultural Diversity on Non-adherence

Chair: Carolyn Tucker, Ph.D., Professor, Department of Psychology, University of Florida, Gainesville, FL

Treatment Concordance: The Patient-Health Care Team Continuum and Its Impact on Non-adherence

Chair: Dr. Dobbels

Strategies to Enhance Treatment Adherence in the Adolescent With Chronic Illness

Chair: Dennis Drotar, Ph.D., Director of the Center for Adherence Promotion and Self-Management, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Tuesday, September 23, 2008

**THE PERSPECTIVE OF PATIENTS AND PARENTS ON TREATMENT ADHERENCE
(PANEL PRESENTATION AND DISCUSSION)**

Moderator: Richard Fine, M.D., Dean, School of Medicine, Stony Brook University Medical Center, Stony Brook, NY

Panel Members: Dr. Barbara Anderson; Jeff Hitchcock, Creator and Webmaster, Children With Diabetes, Hamilton, OH; Allison Tong, Ph.D., M.P.H., Research Officer, The Children's Hospital at Westmead, Sydney, New South Wales, Australia

Dr. Tong, who performs research with parents of children with CKD, told the workshop participants that these children depend on their parents for complex, continuous, and intensive support. The parents face heavy psychosocial, physical, and financial challenges. They may have to deliver home-based medical interventions such as dialysis and enteral feeding and require the child to follow strict liquid and diet restrictions. Qualitative research has shown that these parents are particularly burdened by: (1) struggling to adhere to liquid and diet restrictions while providing the child with adequate nutrition, and (2) adhering to the medical regimen, observing symptoms, and feeling concerned about the child's appearance, education, and development. In-depth interviews with parents of 20 children with CKD have revealed that the medicalizing of parenting is one of the most important issues that these families face. Parents expressed concern about side effects and about the need to distance themselves from the child's experiences, in many ways acting more like a nurse than a parent. Psychologically, parents find withholding of water from the child to be especially difficult.

Dr. Tong said that qualitative studies of the experiences of adolescent organ transplant recipients have shown that managing medical demands is a major issue for these young people because it involves pain and discomfort, requires them to assume responsibility, makes them dependent on caregivers, disrupts their lifestyle, and requires vigilant adherence for survival. Although health professionals place the highest value on enforcing treatment adherence to achieve better clinical outcomes, CKD parents and patients have other priorities. Parents value relief and comfort for the child, avoidance of side effects, and being able to act as a parent and provide for the child's needs (including such basic needs as water, which must often be restricted in CKD patients). Patients value peer acceptance, having a normal appearance, a sense of normality, having control, opportunities for emotional venting, and their current, immediate health status. The three groups—professionals, parents, and patients—need to collaborate and compromise to develop strategies and solutions that will lead to the best outcomes.

From his perspective as a parent of a child with type 1 diabetes, Mr. Hitchcock said that it is important to set up children with diabetes to succeed rather than to fail. Even the diagnosis experience should be a positive one, if possible. Families need to learn to regard blood sugar values as neither good nor bad, but rather as useful data that guide diabetes management. Mr. Hitchcock pointed out that diabetes management is not rocket science; it is much more difficult than rocket science. In addition to coping with the complexities of disease management, parents need to be vigilant in every interaction with their children to avoid hostile confrontations and the

descent into learned helplessness. It may be helpful for parents to think of themselves as coaches. Their role is to help their children learn to play the diabetes “game.” Successes are the “players’,” and when things do not go well, it indicates a need for better coaching.

Mr. Hitchcock founded a website for children with diabetes and their families that has grown into a large and active online community. He believes that its growth is indicative of families’ hunger for knowledge and support. Peer support, especially from peers who are coping well with diabetes, can be helpful for adolescents. The young people tend to self-organize and work among themselves.

Speaking from 30 years of experience working with families coping with type 1 diabetes and 6 years working with those with type 2 diabetes, Dr. Anderson emphasized the importance of communication. Problems develop when well-meaning parents do not know how to talk with their children about diabetes. Shame and blame need to be avoided. Changes in vocabulary, such as referring to blood sugar “monitoring,” “checking,” or “surveillance” rather than “testing,” are helpful because they make the situation less judgmental. It is important for providers to give families hope at diagnosis by letting them know that others have coped well with diabetes and that they can too; to model appropriate communication; and to teach parents how to communicate effectively with their children. Parents also need to be given a realistic idea of how much work is involved in diabetes management so that they do not feel that they have failed when the process proves to be challenging and time-consuming.

Dr. Anderson noted that diabetes management may deteriorate during the college years. The care provided by the college health service may be insufficient, and college students who have had negative experiences with pediatric diabetes care (such as feeling that they could “never do anything right”) may not be motivated to make the effort to seek the care they need.

Dr. Anderson advised that health care providers need to focus very carefully on the timing, tone, and intensity of their communications with families and patients during times of transition or crisis, such as immediately after diagnosis, when families are particularly vulnerable. One important message to communicate is that staying healthy now, through good diabetes management, should enable the child to take advantage of improvements in diabetes care—possibly even a cure—when they become available in the future. Despite the cognitive limitations of adolescents, they can be motivated by a focus on both their present and future health.

Dr. Fine summarized the preceding presentations and added some suggestions from the research standpoint, as follows:

1. Engagement, education, and support of parents are crucial and require continuous rather than episodic involvement.
2. The focus must be on the patient’s successes, avoiding reprobation.
3. The importance of peers should be recognized, and opportunities to connect children with chronic diseases with one another should be provided, perhaps online. However, some sort of surreptitious supervision of these communications is needed to avoid the sharing of dangerous misinformation.

4. The possibility of taking parents and patients out of the adherence equation should be considered if technology permits it. For example, this might be possible with the use of self-monitoring insulin pumps for patients with diabetes. Similarly, for organ transplant patients, the ideal would be to make the patients tolerant and stop their drugs, thus removing the need for adherence to immunosuppressant medication. In lieu of that, intravenous drugs might be given periodically to avoid the need for adherence to oral medications. Also, there is a need to look at transplant patients who kept their organs for long periods of time despite non-adherence to immunosuppressant medication and try to determine what worked for them.

Discussion

Dr. Warady asked Dr. Fine to provide a physician's perspective on addressing the problems of communication and adherence. Dr. Fine said that parents with attitudes like Mr. Hitchcock's make a physician's life easier. Many families, however, are socially and financially very disadvantaged and do not have access to optimal resources. Communication should be a hallmark of the relationship between the physician and parents/patients, to gain their understanding of the disease process. Physicians need to listen to parents and patients to find out what they perceive to be their most important problems, rather than imposing their own ideas, and they need to be aware of what resources are available. If studies test interventions that require ample resources but similar interventions would be impractical in the community because resources are limited, the results of the studies are of questionable value. It may be important to conduct studies to determine the minimum resources needed for success.

A participant commented that technological solutions to adherence problems may have downsides because pumps and monitors have problems of their own. He also asked when supporting a family that is doing less than is necessary shades into enabling. Mr. Hitchcock said that it is important to emphasize that diabetes care is not optional. Enabling suboptimal care is not the goal; the goal is to help people succeed in achieving good care. Dr. Anderson said that one of the difficulties between enabling and helping involves setting goals and assisting patients with breaking formidably large tasks into realistic smaller "bites." Providers should maintain high expectations but not browbeat patients or accept poor care.

Ms. Mariaelena Calhoun expressed the view that all patients with type 1 diabetes should be on insulin pumps and that life with diabetes should be "normalized" for children and families from the time of diagnosis. One of the biggest tasks at hand, in her opinion, is making the constant vigilance required for the management of type 1 diabetes self-motivating, even for families with limited resources. Dr. Fine agreed that interventions need to be designed to be effective for the lowest common denominator in terms of family resources, not the highest, and that modern technology should be used, although he does not believe that every patient should necessarily be on an insulin pump.

Dr. Ferris commented that parents do not need to be highly educated to be effective in helping their children adhere to treatment recommendations for chronic illnesses. In her experience, some parents of children with CKD who are illiterate or who do not speak English have been able to manage well, and much can be learned from their successes.

A participant asked Dr. Ferris about her personal experience as the parent of a child with CKD. Dr. Ferris replied that it was a difficult experience, even an overwhelming one, even though she was a medical student at the time of her child's diagnosis. Helping her son transition to adult care was one of the most difficult situations because no guidance was available on how best to accomplish it. In Dr. Ferris' view, all health care providers have to play somewhat of a parental role with their patients with chronic diseases, and providers should structure interviews with patients in a way that allows them to admit to human behaviors (e.g., "When was the last time you had sex?" rather than "Do you have sex?").

Dr. Guttman-Bauman raised the issue of the discrepancy between needs and resources in diabetes care, noting that it is difficult to get sufficient support services because of Medicaid restrictions and because insurers resist new programs. Better measures of outcomes will help to provide the data needed to justify requests for reimbursement.

Dr. Fine stated that he supports the concept of a medical home, which can advocate for families by getting the resources they need. There is a need for advocacy for change in the way in which resources are provided. One especially difficult situation pertains to organ transplant recipients, who may lose their health insurance at age 21 years, but there has been little effort to rectify this situation.

Dr. Tucker recalled her own experience as a patient on temporary hemodialysis in an acute situation, noting that she was very non-adherent, at least in part because she felt no connection with her nephrologist. This situation prompted her interest in research on patient/provider interactions. There is evidence of differences in the quality of providers' interactions with African American and white patients, with the quality and tone of the interactions being more negative for the African Americans. Dr. Tucker stated that her own research indicates that patient ratings of provider behaviors predict outcomes, including adherence outcomes, and that issues of personal control and trust in providers are stronger predictors of outcomes in African Americans than in whites. The challenge is to get providers to participate in training to modify their own behaviors; often, they are too busy to do so. Dr. Fine stated that medical schools should teach cultural competency and test for it. A recent conference in Tampa on non-adherence in transplantation recommended that all providers should have mandatory cultural competency training. Dr. Tucker noted that culturally sensitive health care requires more than cultural competence. Dr. Mohammad Malekzadeh expressed the view that cultural competency should be part of continuing medical education.

A participant said that she was struck by all the things that families have to manage and wondered how families could "put the illness in its place" and maintain family life. Mr. Hitchcock said that there is no easy answer. His family found it possible to compartmentalize diabetes care to some extent, but parental worry never goes away. Dr. Anderson noted that "putting the disease in its place" will not happen overnight. Parents of a child newly diagnosed with a chronic disease face many "firsts," and it is not until they have acquired some experience in dealing with the disease that they can achieve a new "normal" state for their families.

Dr. Moxey-Mims asked Dr. Tong about the priorities for her ongoing research on the needs of CKD providers, parents, and patients. Dr. Tong said that she hopes to develop interventions

including school-based peer programs and that she is working to learn more about adolescent perspectives on how to improve their quality of life.

Returning to the issue of racial differences in experiences with the health care system, one participant said that he has not observed it but that the quality of the provider/patient interaction may depend on the extent to which parents ask questions and interact with the provider. He also observed that the burden of a medical treatment regimen, particularly in CKD, may well be too extensive for some parents. Dr. Tucker observed that the lack of questions from some parents may be an indicator that they are too intimidated to ask, rather than that they do not have any questions.

Dr. Elaine Kamil observed that cultural competency is a two-way street. Families need to accept providers from backgrounds different from their own, and providers may need to help them learn to do this. Dr. Sandra Amaral noted that cultural competency training should include other staff members, such as transplant coordinators, as well as health care providers, and that interactions with patients should focus on identifying barriers to non-adherence rather than on blame. Dr. Fine noted that it may be helpful to take the approach that if the patient is non-adherent, it is the health care team's problem—that their efforts have not been effective in some way—rather than blaming the family and patient.

A participant observed that research hypotheses need to be specific, that interventions must be reasonable in cost, and that if resources are minimized, patients with the greatest needs will not have those needs met. Dr. Fine observed that the financial cost of non-adherence is very high—\$300 billion annually in the United States for all diseases. A participant noted that disparities in outcome reflect differences in power, a situation that may need to be changed through advocacy and the collective addressing of grievances. Health care providers may need to join politically with patients on key issues.

Dr. Drotar observed that provider/parent/child transactions are highly charged and complex and asked whether it would be helpful to empower parents to deal with medical culture. Dr. Anderson explained that the Joslin Diabetes Center has established a Care Ambassador program to help guide families through the health care system and has found that it decreases poor outcomes and reduces costs. Another participant noted, however, that attempting to empower families without making appropriate changes in the health care system could set up families for failure.

Dr. Fine stated that it is important to focus on the role of peers in adolescent behavior and involve peers in the adherence process. In his opinion, interventions designed to improve adolescent adherence should incorporate peers.

INTERVENTIONS TO PROMOTE TREATMENT ADHERENCE

Moderator: Mike Rapoff, Ph.D., Professor, Department of Pediatrics, University of Kansas Medical Center, Kansas City, KS

Lessons to Be Learned From Adult Intervention Studies

Jacqueline Dunbar-Jacob, Ph.D., R.N., F.A.A.N., Dean, School of Nursing, and Professor of Nursing, Psychology, Epidemiology, and Occupational Therapy, University of Pittsburgh, Pittsburgh, PA

Dr. Dunbar-Jacob summarized what is known and what still needs to be learned about non-adherence in adults. She noted that 45 percent of all Americans have some chronic disease, including 22 percent who have two or more chronic diseases, and that about 40 to 50 percent of adults with chronic health problems are non-adherent, a percentage that has been stable since adherence research began in the 1960s.

To date, there have been 78 randomized, controlled, long-term (6 months or longer) trials of adherence interventions in adults, testing 92 total interventions. Fewer than one-half of these interventions improved adherence, and only about one-third improved clinical outcome. Moreover, even when statistically significant positive effects were observed, the effect sizes were consistently modest. The highest success rates have come from complex, multicomponent interventions that included both educational and behavioral components, with frequent contact with the patients throughout the study.

Most clinical trials of adherence have focused on a single disease and one or more components of its treatment regimen, but accumulating evidence indicates that the number of co-morbidities influences adherence. Very little research has focused on good adherers and the factors that allow them to be successful. Developing better evidence on this topic could provide clues about how to design interventions for individuals who are poorly adherent.

In general, sociodemographic factors have not proved to be consistent predictors of adherence in adults; relationships have varied from study to study. Disease and treatment characteristics appear to be more important than sociodemographics. The number of co-morbidities, the number of medications, and the number of times a day that medication must be taken are all correlated with adherence, and there is evidence that adherence declines over time. Studying adherence to one treatment does not give a full picture of an individual's adherence to a complete treatment regimen or even of adherence to similar components of multiple treatment regimens. For example, adherence to medication for one condition (e.g., hypertension) is not a good predictor of adherence to medication for another condition (e.g., diabetes) by the same individual.

Measurement is an important issue in adult adherence studies. The correlation between adherence measured by one method (e.g., self-report) and another method (e.g., electronic monitoring) is low, and factors that correlate with adherence as measured by one method may not correlate with adherence measured by another. For example, in one trial, depression was correlated with self-report adherence but not with adherence determined by electronic

monitoring. Thus, researchers must be careful to state what kind of adherence measure they used when reporting conclusions.

Discussion

Dr. Rapoff commented that there is much that researchers working on adolescent adherence can learn from the adult adherence literature. The issues of measurement and co-morbidities that have proved important in adults apply to adolescent patients as well.

Meta-analysis of Psychological Interventions to Promote Adherence to Treatment in Pediatric Chronic Illness: Implications for Future Research

Dr. Drotar

Dr. Drotar described the results of a recent meta-analysis of psychological interventions to promote treatment adherence in pediatric chronic illness, including type 1 diabetes. The studies included in the meta-analysis did not focus specifically on adolescents, although some adolescents were included. All of the studies assessed the effects of psychological interventions on quantifiable measures of treatment adherence, and some included measures of clinical outcomes as well. Overall, stronger effects were found for behavioral and multi-component interventions; educational, psychosocial, and technology-based interventions were less effective.

Among children and adolescents with type 1 diabetes, effect sizes were relatively small, and behavioral, technological, and psychosocial interventions were the most effective. Effect sizes varied for different domains of adherence, with the smallest effects for dietary change. Of 10 studies that assessed effects on HbA1c, six showed no overall effects, and four showed significant effects. One study showed a reduction in hospitalizations for ketoacidosis.

In general, the results of the meta-analysis indicated that effective psychological interventions should: (1) be highly structured, (2) target relevant adherence behaviors, (3) be family centered, (4) include both educational and behavioral components, and (5) use technology as applicable. The studies currently available are limited by the frequent use of subjective assessments of adherence and brief periods of follow-up. Also, it is often difficult to pinpoint the specific factors that accounted for change in these studies or to determine whether the changes in adherence were clinically significant, and some of the tested interventions have been of limited relevance to the usual clinical situation. Dr. Drotar recommended that future studies should standardize measures of adherence, identify the most effective components of multifaceted interventions, and study mediators of change. The use of longer follow-up periods and a greater focus on high-risk populations are also needed. Studies should be designed with sufficient power to detect changes in HbA1c as well as adherence and should evaluate interventions delivered in clinical settings.

Innovative Approaches for Interventions and Outreach to Promote Adherence in Youth With Diabetes

Dr. Laffel

Dr. Laffel stated that innovative approaches to adherence and outreach are needed because adolescents are not currently meeting treatment goals and because poor diabetes control and infrequent follow-up increase the risk of complications.

The poorest outcomes in terms of HbA1c values are found in patients aged 11 to 20 years. Data from 18 technologically advanced countries show that HbA1c has not budged during a decade of follow-up. The data also show that the younger the age at diagnosis of type 1 diabetes, the more difficult it is to control BG throughout life, which may reflect biology as well as behavior.

The use of insulin pumps has increased exponentially in recent years. This technology has posed new challenges because rates of non-adherence doubled with the introduction of pumps. An intervention in which pumps were equipped with meal bolus alarms to enhance adherence worked for only 3 months, after which patients tended to turn the alarms off and returned to their previous rates of non-adherence.

New challenges may be coming with the introduction of continuous glucose monitoring. One study has shown improved glycemic control with continuous monitoring in patients age 25 and older but no significant improvement in those aged 8 to 14 or 15 to 24 years. This likely reflects less frequent wearing of the continuous monitoring devices in the younger groups, particularly 15- to 24-year-olds who, not coincidentally, had the poorest HbA1c values.

The challenges of continuous glucose monitoring for families and adolescents with type 1 diabetes include the following:

- Parents seek improved approaches to care and provide consent; adolescents merely “go along for the ride.”
- Adolescents expect the devices to make management easier and may have unrealistic expectations for a “cure.”
- Parents decrease their involvement in their children’s care during adolescence because of increased adolescent autonomy and need for privacy (the latter is a particular problem with monitoring devices because the sensor is worn on the body and adolescents may therefore perceive parental involvement with its use as a personal invasion).
- Parents of younger children often fear low BG values more than high ones.
- Children do not look at the receiver, and adolescents often ignore “nuisance” alarms.

Dr. Laffel concluded by observing that family involvement is necessary for successful adherence to diabetes treatment programs, including the use of new technologies.

Discussion

A participant asked Dr. Laffel about the best ways to target adolescents with diabetes who are non-adherent because they are fearful of gaining weight. Dr. Laffel replied that it is important

for patients to understand that insulin does not promote weight gain—food does. There is a need for research on disordered eating in people with diabetes.

Top 10 Ways to Advance Pediatric Medical Adherence Research

Dr. Rapoff

Dr. Rapoff proposed and discussed 10 ways to advance research on pediatric medical adherence, particularly assessment and intervention, as follows:

1. Settle on standard terminology and definitions.
 - The old standby definition of adherence as the extent to which a person’s behavior coincides with medical or health advice has the benefits of focusing on specific regimen-related behaviors, implying quantitative and qualitative differences in adherence, and focusing on the concordance between what patients are asked to do and what they really do. Newer definitions that incorporate the concept of “agreed recommendations” may also be valuable, however.
2. Develop standard scores and cutpoints for defining “acceptable” adherence derived from adherence measures.
 - Currently, a variety of different standards are used, which contributes to confusion. Ideally, acceptable adherence should be defined on the basis of biologic criteria, that is, on what minimum level of adherence is needed to obtain therapeutic effects for a particular regimen.
3. Revise, rework, and make adherence theories relevant to pediatrics.
 - Theories are valuable because they help researchers conceptualize and approach adherence issues, influence decisions made in the planning and conduct of studies and in the reporting of data, and meet the needs of grant review panels, which require a theoretical rationale for studies.
4. Develop reliable, valid, sensitive, and practical self-report measures of adherence.
 - To encourage accurate reporting, such self-report measures should acknowledge and normalize behavior that is less than perfectly adherent. Parent reports of children’s adherence are more valid for younger children; self-reports are more valid for adolescents.
5. Continue the development of electronic measures of adherence.
 - Such measures are useful not only in research but also in interventions. The individualized information they generate can help providers, parents, and patients problem-solve to find ways to overcome barriers to adherence.

6. Develop and standardize practical measures of disease activity and quality of life.
 - The ultimate goal of adherence research is that patients feel better, get better, and do better. To achieve this goal, it is necessary to have data on changes in symptoms and quality of life. Automated, daily assessments, perhaps performed online, may be helpful.
7. Validate primary and secondary interventions to prevent or minimize anticipated declines in adherence over time.
 - Primary interventions would target patients who are not yet exhibiting clinically significant non-adherence, using educational and behavioral interventions, and simplifying regimens when possible. Secondary interventions would target patients who have recently become non-adherent and would use strategies such as more frequent monitoring of adherence, positive social reinforcement, and routine discipline strategies. Pediatric psychologists have important roles to play here, both in training nurses and other health care providers to implement interventions and in working directly with the children and adolescents with the most serious problems.
8. Make better use of single-subject design methodology, given the small samples available at most sites.
 - Single-subject designs can be useful in identifying effective and ineffective interventions.
9. Develop and test innovative adherence promotion strategies and ways to deliver interventions.
 - For some diseases and interventions, standard lists have been developed in which parents or children identify specific barriers (such as forgetting to take medicine or disliking the taste of medicine) that apply to them. The information obtained in this way can then be used in focused problem-solving. Prompting devices originally designed for elderly patients may be useful for adolescents for whom forgetting to take medications or refill prescriptions is a barrier to adherence.
10. Conduct multisite, randomized, controlled adherence intervention trials.
 - Funding is needed for behavioral studies, just as it is for medical studies.

REPORTS FROM BREAKOUT GROUPS

Moderator: Dr. Warady

The reports of the individual workgroups were presented by the chairs of each group, except for the group chaired by Dr. Wysocki, for which the report was presented by Dr. Kristen Riekert of the Johns Hopkins School of Medicine in Dr. Wysocki's absence.

The Influence of Ethnic and Cultural Diversity on Non-Adherence

Dr. Tucker

This workgroup proposed five research ideas, as follows:

1. Research is needed to identify factors that account for adherence differences between the following groups of adolescents with chronic illness:

- Those in low-income versus middle- to high-income families.
- Those in families with one versus two or more primary caregivers.
- Those self-identified as members of minority groups versus those not so identified.

This research ideally should include:

- Assessment of the views of health care providers regarding factors that account for group differences.
- Investigation of biological and associated environmental factors that might account for group differences.

2. Research is needed to identify contributors to treatment non-adherence among non-adherent adolescents who live in vulnerable families (those in any of the three groups identified above). This research should primarily be qualitative, with adolescents, family members, and providers all sharing their perspectives.

3. Studies of ethnically and culturally diverse adolescents who are treatment adherent are needed, to identify both common and ethnicity- and culture-specific factors that promote or account for adherence. Ideally, these studies should include qualitative components.

4. Research is needed that investigates the impact of the following on adolescent non-adherence:

- Forging positive relationships among individuals involved in treatment (e.g., patient-provider-primary caregiver relationships).
- Involving providers, adolescents, and family members in training designed to modify/prevent treatment non-adherence, increase health promoting behaviors, and promote positive health outcomes in these adolescents.
- Connecting adolescents with health- and treatment-promoting resources in their communities.
- Exposing adolescents to youth-generated media designed to promote adherence and healthy lifestyles.

5. There is a need for community participatory research and ecological model-based research that aims to understand and modify non-adherence and promote healthy lifestyles and positive health outcomes among ethnically and culturally diverse adolescents with chronic illness.

The Role of the Family in Adolescent Treatment Non-Adherence

Dr. Riekert for Dr. Wysocki

This workgroup identified several research questions in five areas, as follows:

1. Helpful versus non-helpful parenting, with a focus on an empowerment versus deficit model
 - What parenting practices are used by families to help their adolescent successfully adhere to a regimen? (It should not be assumed that this is the opposite of the parenting practices used in families who are doing poorly.)
 - How do some families adhere adequately despite facing numerous risks?
2. Family-health care provider interactions
 - Are the long-term complications of non-adherence communicated to the parent and child? If so, when and how? Does this communication affect adherence?
 - What role does health care provider communication play in facilitating adolescent adherence to a regimen?
3. Issues of emerging adulthood
 - How the process of transition is completed and how does this affect adherence? Are health care providers who treat adults knowledgeable about the developmental aspects of emerging adulthood?
 - What can families do to support adherence yet respect normal developmental maturation?
4. Integration of psychosocial professionals into medical care
 - What is the value of providing anticipatory guidance as a strategy to prevent non-adherence?
 - What are the best practices for offering individualized psychosocial services in a personalized way to the largest number of patients? Would the use of “Ph.D. extenders” (i.e., psychological professionals with a lower level of training) be cost effective? How can telemedicine and the Internet be integrated into adherence promotion?
5. Translational research
 - How can empirically validated interventions be adapted for broader implementation into community-based clinical practice?
 - How can efficacy studies be better designed to facilitate the dissemination of interventions to the broader community? Should the focus be on studies of practical effectiveness rather than efficacy?

Treatment Concordance: The Patient-Health Care Team Continuum and Its Impact on Non-adherence

Dr. Dobbels

In their discussions, this workgroup agreed that because non-adherence is a multifactorial problem, a multidimensional approach is indicated, targeting as many risk factors as possible. A multi-level approach is also indicated, targeting not only the patient but also the health care provider, the health care facility (such as a transplant center), and even health care policy.

The workgroup developed the following ideas for future studies:

1. Evaluate training in motivational interviewing as an adherence skills toolkit for health care providers. This would involve:
 - Updating an existing meta-analysis on the efficacy of motivational interviewing as a behavior change agent.
 - Performing a multicenter randomized controlled trial to test the efficacy of health care team training in motivational interviewing on adherence and clinical outcomes.
 - Performing a randomized controlled trial to test the effects of different amounts of training.
 - Conducting translational research to stimulate health care providers to use motivational interviewing in clinical practice.
2. Develop a more streamlined way to assess and address barriers to adherence. This would require:
 - Developing a comprehensive instrument to assess barriers.
 - Conducting a prospective cohort study to investigate barriers, adherence, and outcomes simultaneously.
 - Developing technology to assess barriers in routine clinical practice and to assess its usability and acceptability.
 - Conducting a clinical trial to assess whether the efficacy of using technology to add prompts based on identified barriers improves adherence and clinical outcomes.
3. Determine ways to encourage and train providers to implement a chronic illness management/patient-centered approach. Steps would include:
 - Devising and validating an instrument to assess chronic illness management.
 - Conducting a field study to evaluate which communication patterns have a positive or negative impact on adherence.
 - Conducting a multicenter study to assess whether different levels of chronic illness management have different impacts on adherence and clinical outcomes.
 - Developing and testing the efficacy of interventions to improve communication with parents and patients.

4. Examine resilience factors in adherent adolescents and their families by conducting qualitative research to evaluate what helps patients and families to be adherent, with the results of this research being used to guide future intervention studies to improve adherence in non-adherent patients.
5. Identify patient and family needs with regard to communication. This would entail:
 - Conducting qualitative research to evaluate what patients expect from the health care team.
 - Developing and testing an intervention in which patients and parents would learn how to better interact with health care providers.

Strategies to Enhance Treatment Adherence in the Adolescent With Chronic Disease

Dr. Drotar

This workgroup proposed testing a variety of interventions of two types: those focused on the adolescent and the family, and those focused specifically on the adolescent:

Adolescent and Family Focused

1. Test interventions that are designed to enhance treatment adherence and self-management by promoting resilience in adolescents with chronic illness and their families.
2. Study the efficacy of interventions that are designed to lessen the treatment and illness burden experienced by families of adolescents with chronic illness to enhance treatment adherence.
3. Study and evaluate innovative interventions to promote adherence to treatment among targeted populations of adolescents with chronic illness and their families (e.g., adolescents and families at high risk for treatment non-adherence or experiencing clinically significant problems in adherence).

Adolescent Focused

4. Test interventions that enhance social support, especially peer support, for adolescents with chronic illness to enhance treatment adherence and self-management (e.g., peer groups, peer mentorship, peer support in camp settings).
5. Develop and test interventions that educate and support families and adolescents to promote treatment adherence during critical developmental transitions (e.g., onset of adolescence, transition to adulthood).
6. Test the efficacy of innovative methods designed to help adolescents develop and sustain motivation for treatment adherence and self-management (e.g., motivational interviewing, use of technology such as text messaging and web-based interventions).

7. Evaluate the stability of the effects of adherence promotion interventions on adolescent self-management and relevant clinical outcomes (e.g., HbA1c, symptom control, health-related quality of life).
8. Evaluate the effects of interventions designed to promote treatment adherence and self-management in adolescents in understudied chronic illness groups (e.g., renal disease, digestive diseases including inflammatory bowel disease).
9. Test interventions that provide provider-focused support and education for health care providers. Improve adherence to guidelines, communication with families, and adolescent adherence promotion efforts.
10. Evaluate the efficacy of innovative methods of managed care and reimbursement for health care providers to promote and sustain adherence promotion interventions.

CLOSING REMARKS

Dr. Warady

In closing, Dr. Warady stated that the meeting had been very successful in achieving its goals of reviewing the literature on adolescent non-adherence, sharing experiences and opinions, and generating research initiatives. He said that it was especially beneficial to have this forum in which experts from different disciplines could get together and talk about the same patient population, and he expressed hope that the research to be conducted as a result of the initiatives generated here would be practical and clinically applicable. Dr. Warady thanked the planning committee for organizing the conference, and he thanked the NIDDK for sponsoring the conference and for its commitment to the challenge of non-adherence.