

Promoting Medication Adherence in Children

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The problem of getting children to follow a treatment regimen is widespread and is frustrating for physicians. The extent to which any patient adheres to a medical regimen is an essential determinant of clinical success. Strategies to improve adherence in children include using simplified drug regimens (e.g., once-daily dosing), pleasant-tasting medicines, liquid or other nonpill formulations, regular phone contact between parents and physicians, reminders, information counseling, self-management plans, and other forms of individualized supervision or attention. Physicians also can encourage adherence by providing a clearly written explanation or patient information sheets that list generic and brand names, dosage, schedule, duration, and common side effects and practical ways of coping with them. Physicians, children, and parents should develop a mutually agreed-upon treatment plan. Having the child participate in devising the plan improves adherence. (*Am Fam Physician* 2006;74:793-8, 800. Copyright © 2006 American Academy of Family Physicians.)

► **Patient information:** A handout on giving medicine to children, written by the authors of this article, is provided on page 800.

ACF This article exemplifies the AAFP 2006 Annual Clinical Focus on caring for children and adolescents.

Physicians and their colleagues have considerable difficulty in understanding and managing poor adherence to medications. One major frustration for physicians is caring for children with acute or life-threatening illnesses who do not adhere to their treatment plans. It is even more difficult for physicians to understand when parents do not provide optimal care for their children. Approximately 30 to 70 percent of patients with chronic illnesses have poor adherence because of extended treatment duration, multiple medications, and periods of symptomatic remission.¹⁻³ Clinical experience indicates that poor adherence is common in patients with chronic illnesses (e.g., cystic fibrosis, epilepsy, asthma, diabetes).

With the advances in medical therapeutics during the past two decades, it seems reasonable that nonadherence studies or research on effectiveness strategies in children would flourish.⁴ On the contrary, the literature concerning interventions to improve medication adherence remains surprisingly weak. Compared with the thousands of trials for individual drugs and treatments, there are few relatively rigorous trials of adherence interventions.⁵ The Cochrane Database of Systematic Reviews has identified

several effective interventions for improving medication adherence, including more convenient care (e.g., regular phone contact with the physician), reminders, information counseling, self-management plans (e.g., self-monitoring with regular medical review and a written action plan), reinforcement, and other forms of supervision or attention. In these reviews⁶⁻⁸ the researchers concluded that, even with the most effective methods, the improvements in health or medication adherence were not large.

Tips for improving adherence to medication are listed in *Table 1*. Data flow sheets and more convenient once- or twice-daily drug administration are associated with compliance rates of greater than 70 percent.⁹⁻¹²

Barriers to Medication Adherence

For parents and children, the daily hassles of living, stress, and typical family conflict are the biggest barriers to medication adherence.¹³ Reasons why children do not take their medications include parents' lack of understanding of the diagnosis, concerns about drug therapy effectiveness, and fear of medication side effects. This is especially true in children with chronic diseases. One survey of parents of children with asthma found that parental concerns about controller medication were

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
When feasible, use once- or twice-daily medication schedules, because this increases compliance rates to greater than 70 percent.	B	12, 26
When prescribing medications to children, give the parent educational materials to improve adherence.	C	1
Use sweeteners, chocolate flavoring, or chocolate chasers to mask bitter medications and to improve a child's willingness to take medicine.	B	21, 22

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 699 or <http://www.aafp.org/afpsort.xml>.

associated with poor medication adherence.¹⁴ For example, the parent of a child with asthma may stop a daily inhaled steroid when the child is feeling better, hoping that this will prevent the adverse effects of the medication.

Age, socioeconomic status, race, and family factors also can influence adherence to treatment, especially in children with asthma, epilepsy, and diabetes.^{15,16} On average, parents forget one half of the information presented to them during a 15-minute meeting with a physician. Most of the information

retained is associated with the diagnosis and generally is presented during the first third of the discussion.¹⁷

**Increasing Adherence in a Young Child
ILLUSTRATIVE CASE**

A nine-month-old girl presents with fever, irritability, rhinorrhea, and a red bulging tympanic membrane in her right ear. Because her last episode of otitis media was six months ago, amoxicillin is prescribed (three times daily for 10 days). Her mother primarily speaks Spanish but is able to explain that in the past her daughter had cried and spit out the medicine. Because of the language barrier, there is concern about the inability to communicate the importance of finishing all of the medication.

DISCUSSION

Medication adherence is a complex issue involving the child, family members, and other caregivers. This process is dependent on the family's cultural beliefs, their perceptions of disease severity, and their understanding of the benefits of treatment. Patients often construct their own versions of adherence according to their personal worldviews and social contexts.¹⁸ Language barriers and low health literacy have been shown to be obstacles to adherence. Interpreters, bilingual staff, reinforcement of instructions by pharmacists or nurses, medication technique training (e.g., inhaler, injection, or dropper use) are helpful tools. Today, translated patient information sheets can be found on the Internet, in local pharmacies, through pharmaceutical companies, and through private translation services (Table 2). Patient education publications have been shown to reduce adverse drug events related to noncompliance.¹

TABLE 1
Tips for Improving Medication Adherence in Children

For physicians

- Prescribe medications that can be given once or twice daily.
- Have others (e.g., pharmacists, nursing staff, medical assistants, subspecialists) reinforce the information.
- Provide patient information handouts.
- Renew medications regularly.*
- Keep clear documentation in the patient's chart (e.g., contracts, reevaluation policies).
- Discuss medication safety issues with the patient's parents.
- Consider the financial cost of medications (prescribe generics when possible).

For patients

- Incorporate dosing into daily routines and take medication at the same time each day (e.g., after brushing teeth, before a meal).
- Keep a tally sheet of doses, mark a calendar, or use a pillbox.
- Use visual reminders (e.g., notes on the medicine cabinet or refrigerator).
- Ask a friend or family member to remind you.
- Set an alarm on your clock or watch.
- Use a paging system with a beeper.
- Parents can offer children rewards (e.g., stickers, small toys) for remembering.

*—Many insurers charge more if maintenance medications are prescribed for less than three months.

Special considerations for younger children include dosing and administration of liquid medications, oral suspensions, and chewables; the taste of medicine; and administering medications in school or day care.¹⁹ Table 3 lists medications commonly prescribed to children, their side effects, and their dosing methods. It is important to remind parents that regular eating utensils (e.g., spoons) can differ in volumes, causing inaccurate dosing. If there is a concern, write a request on the prescription for the pharmacist to provide a dispenser (e.g., medicine syringe, measuring spoon) or provide the patient with a dispenser during the office visit. A recent study²⁰ showed that a color-coding chart and medication dispenser reduced dosing errors. Mixing medication with a small amount of food or juice, using rewards, or other strategies might help increase compliance in young children.

Adding sweeteners to foods or products given to children may have a positive effect on compliance and feeding patterns.²¹ Children have varying preferences toward different antibiotic tastes, and introduction of additional flavors may improve compliance. Several reports show that chocolate flavoring or chasers often are preferred because they effectively mask the taste of bitter medications.²²

Another method of increasing compliance is to increase palatability of suspensions (by refrigeration or other means). Many companies provide specialized flavoring services, where an additional flavoring is added to medications. Some companies (e.g., Flavorx [<http://www.flavorx.com>]) are located in hospitals and community pharmacies.

Increasing Adherence in a School-age Child

ILLUSTRATIVE CASE

A 10-year-old obese boy with poorly controlled asthma, who uses several inhalers, presents for a routine follow-up visit. His parents appear confused by the different recommendations from his multiple health care providers (i.e., primary care physician, pulmonologist, school nurse) and are uncertain which inhalers he should take to school. Because of his poor pulmonary function

tests, there is concern about his inhaler use. The family physician and parents discuss putting a school plan in place and having a team meeting with the patient, his health care providers, and his parents.

DISCUSSION

Children with chronic illnesses often have more than one health care provider. Identification and communication among the parents, the various physicians, school nurses, pharmacists, teachers, and guidance counselors is essential, and the creation of a school management plan often is necessary. Such a plan usually includes prescription and over-the-counter medication dosing information, triggers, signs and symptoms to be aware of, and emergency phone numbers.²³ All members of the health care team should be actively involved in the treatment (e.g., nurses and pharmacists are trained to counsel patients

TABLE 2

Patient Information Resources for Medication Adherence

20 Tips to Help Prevent Medical Errors (AAFP)	http://www.aafp.org/fpm/20020700/49_box_a.html
Allergy & Asthma Medication Guide (AAAAI)	http://www.aaaai.org/patients/resources/medication_guide
Be an Active Health Care Consumer (AHRQ)	http://www.ahrq.gov/path/beactive.htm
Children's Health/Medications (AAP)	http://www.medem.com/MedLB/articleslb.cfm?sub_cat=27
Drug Information Online	http://www.drugs.com
Facts for Families (AACAP)	http://www.aacap.org/publications/factsfam/index.htm
How to Give Medicine to Children (FDA)	http://www.fda.gov/fdac/features/196_kid.html
Youth Zone (ADA)	http://www.diabetes.org/youthzone/youth-zone.jsp
Patient information handouts on various conditions (AAFP)	http://www.familydoctor.org
Your Medicine: Play It Safe (AHRQ)	http://www.ahrq.gov/consumer/safemed/safemed.htm#MedicineandYou

AAFP = American Academy of Family Physicians; AAAAI = American Academy of Allergy Asthma & Immunology; AHRQ = Agency for Healthcare Research and Quality; AAP = American Academy of Pediatrics; AACAP = American Academy of Child & Adolescent Psychiatry; FDA = U.S. Food and Drug Administration; ADA = American Diabetes Association.

Prescribing to Children

on administration of inhalers, injections, diskus, and other medications with difficult administration). It is essential to inform parents and empower them to be an integral part of the team. Addressing family conflicts and introducing targeted interventions to build positive family involvement and interaction around disease management may have a positive effect on medication adherence.^{24,25} Once- or twice-daily dosing are the most

comfortable regimens for school-age children because parents can remind children to take medications or directly observe administration of the therapy.²⁶

As pharmaceuticals are developed and changed, new dosing forms are created (e.g., powders, inhalers, sprinkles, chewable tablets, liquids). For example, the child in the illustrative case might benefit from a combination of an inhaled steroid and

TABLE 3
Prescription Guidelines for Medications Commonly Used in Children

<i>Medication</i>	<i>Formulations</i>	<i>Common side effects</i>	<i>Notes</i>
Amoxicillin	Capsules/tablets, chewables, suspension	Diarrhea, GI upset, rash	Suspension does not have to be refrigerated, but it tastes better cold. Give amoxicillin with or without food. There is greater dosing flexibility with 200- and 400-mg per teaspoon suspensions and chewable tablets.
Amoxicillin/clavulanate (Augmentin)	Capsules/tablets, chewables, suspension	Diarrhea, GI upset	It must be refrigerated. Give it with food. Augmentin ES (600 mg) gives greater dosing flexibility.
Azithromycin (Zithromax)	Tablets, suspension	GI upset	Give suspension at room temperature and on an empty stomach; give tablet with or without food.
Cefaclor (Ceclor)	Suspension	Diarrhea, GI upset	It must be refrigerated. Give it with or without food.
Cefprozil (Cefzil)	Capsules/tablets, suspension	Diarrhea, GI upset	It must be refrigerated. Give it with or without food.
Cephalexin (Keflex)	Capsules/tablets, suspension	Diarrhea, GI upset	It must be refrigerated. Give it with or without food.
Cetirizine (Zyrtec)	Tablets, syrup, chewable	Drowsiness, headaches	Give it with or without food.
Famotidine (Pepcid)	Tablets, suspension	Constipation, diarrhea, rash	Give it with or without food.
Loratadine (Claritin)	Tablets, syrup	Drowsiness, headaches	Give it with or without food.
Metoclopramide (Reglan)	Tablets	Drowsiness, diarrhea	Give it before meals.
Ranitidine (Zantac)	Tablets, syrup	Constipation, diarrhea, rash	Give with or without food.
Trimethoprim/sulfamethoxazole (Bactrim, Septra)	Tablets, suspension	Photosensitivity, GI upset, diarrhea	Give it with or without food.

GI = gastrointestinal.

beta agonist such as fluticasone/salmeterol (Advair Diskus) or a different medication system such as nebulized budesonide (Rhinocort). Sustained-release preparations or preparations with longer or extended half-lives can be used to decrease the number of administrations. For patients taking daily medications, appointment or medication-refill reminders have been demonstrated to improve clinic attendance, an important element of medication adherence.²⁷ As they grow, children are able to more actively participate in the medication management of their disease and in goal setting. It is critical to empower children to learn to take their medications and be responsible for caring for their own health.

Increasing Adherence in an Adolescent ILLUSTRATIVE CASE

A 16-year-old football player comes to the office for a sports physical examination. He has a history of attention-deficit/hyperactivity disorder. His father explains that his son's grades are barely passing this term. If his grades do not improve, he will not be allowed to play football next season. During the examination, the patient says that his mother makes sure he takes his morning dose of methylphenidate (Ritalin), but he often forgets to take his medication during school. The physician decides to start him on a once-daily dosing medication.

DISCUSSION

Sustained-release preparations or preparations with longer or extended half-lives can be used to decrease the number of medication administrations. The new, longer-acting formulations are an alternative to a mid-day medication dose. For example, Concerta and Metadate CD are methylphenidate preparations that provide a more convenient alternative for children with attention-deficit/hyperactivity disorder. At the same time, adolescence is a critical stage when patients need to learn how to manage their own medication, and physicians need to encourage the parents to step back while keeping the lines of communication open. Taking the medication is not negotiable, but determining when

and how to take the medication gives the adolescent a sense of control.

Developmentally, this is a time of increased risk-taking, and patients may resist frequent physician visits or stop taking medication because of the unwanted side effects.² Physicians should be aware that alcohol, illicit drug, and dietary supplement interactions may lead to unwanted side effects and, thus, poor adherence. It is critical to ask every patient about all prescription and over-the-counter medication use and about alcohol, illicit drug, and dietary supplement use.

Parents or health care providers should be especially creative with teenagers; use of contracts, rewards, and peer support groups can be beneficial. In randomized clinical trials, children and adolescents have been found to improve their self-care after playing health education and disease management video games.²⁸

New technologies also are helping improve medication adherence. Electronic monitors are available that measure adherence by detecting actions necessary to administer medications, such as removing the cap from a pill bottle. These monitors store downloadable time- and date-stamped information for up to several months and can provide precise information on the frequency and timing of actual dosing and reveal daily patterns of adherence.²⁹

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REFERENCES

1. Lask B. Motivating children and adolescents to improve adherence. *J Pediatr* 2003;143:430-3.
2. Nevins TE. Non-compliance and its management in teenagers. *Pediatr Transplant* 2002;6:475-9.
3. Haynes RB, McDonald H, Garg AX, Montague P. Interventions for helping patients to follow prescriptions for medications. *Cochrane Database Syst Rev* 2002;(2):CD000011.
4. Costello I, Wong IC, Nunn AJ. A literature review to identify interventions to improve the use of medicines in children. *Child Care Health Dev* 2004;30:647-65.
5. Haynes RB, McKibbin KA, Kanani R. Systematic review of randomised trial of interventions to assist patients to follow prescriptions for medications [Published correction appears in *Lancet* 1997;349:1180]. *Lancet* 1996;348:383-6.
6. Gibson PG, Coughlan J, Wilson AJ, Abramson M, Bauman A, Hensley MJ, et al. Self-management education and regular practitioner review for adults with asthma. *Cochrane Database Syst Rev* 2002;(3):CD001117.
7. Toelle BG, Ram FS. Written individualised management plans for asthma in children and adults. *Cochrane Database Syst Rev* 2004;(1):CD002171.
8. Renders CM, Valk GD, Griffin S, Wagner EH, Eijk JT, Assendelft WJ. Interventions to improve the management of diabetes mellitus in primary care, outpatient and community settings. *Cochrane Database Syst Rev* 2000;(4):CD001481.
9. Clark NM, Gong M, Schork MA, Evans D, Roloff D, Hurwitz M, et al. Impact of education for physicians on patient outcomes. *Pediatrics* 1998;101:831-6.
10. Perez-Gorricho B, Ripoll M, for the PACE Study Group. Does short-course antibiotic therapy better meet patient expectations? *Int J Antimicrob Agents* 2003;21:222-8.
11. Brown CL, Tangsinmankong N, Emmanuel PJ. Improving care of HIV-infected patients in the outpatient setting with patient data flow sheets. *J Assoc of Nurses AIDS Care* 2002;13:58-63.
12. Eisen SA, Miller DK, Woodward RS, Spitznagel E, Przybeck TR. The effect of prescribed daily dose frequency on patient medication compliance. *Arch Intern Med* 1990;150:1881-4.
13. Penkower L, Dew MA, Ellis D, Sereika SM, Kitutu JM, Shapiro R. Psychological distress and adherence to the medical regimen among adolescent renal transplant recipients. *Am J Transplant* 2003;3:1418-25.
14. Conn KM, Halterman JS, Fisher SG, Yoos HL, Chin NP, Szilagyi PG. Parental beliefs about medications and medication adherence among urban children with asthma. *Ambul Pediatr* 2005;5:306-10.
15. Snodgrass SR, Vedanarayanan VV, Parker CC, Parks BR. Pediatric patients with undetectable anticonvulsant blood levels: comparison with compliant patients. *J Child Neurol* 2001;16:164-8.
16. McQuaid EL, Kopel SJ, Klein RB, Fritz GK. Medication adherence in pediatric asthma: reasoning, responsibility, and behavior. *J Pediatr Psychol* 2003;28:323-33.
17. Beers MH. Drug treatment in newborns, infants, and children. In: Beers MH, Berkow R. *The Merck Manual of Diagnosis and Therapy*. 17th ed. Whitehouse Station, N.J.: Merck Research Laboratories, 2004:1961.
18. Sawyer SM, Aroni RA. Sticky issue of adherence. *J Paediatr Child Health* 2003;39:2-5.
19. Dhaon NA. Amoxicillin tablets for oral suspension in the treatment of acute otitis media: a new formulation with improved convenience. *Adv Ther* 2004;21:87-95.
20. Frush KS, Luo X, Hutchinson P, Higgins JN. Evaluation of a method to reduce over-the-counter medication dosing error. *Arch Pediatr Adolesc Med* 2004;158:620-4.
21. Barr RG, Pantel MS, Young SN, Wright JH, Hendricks LA, Gravel R. The response of crying newborns to sucrose: is it a "sweetness" effect? *Physiol Behav* 1999;66:409-17.
22. Schwartz R. Enhancing children's satisfaction with antibiotic therapy: a taste study of several antibiotic suspensions. *Curr Therap Res* 2000;61:570-81.
23. Committee on School Health; American Academy of Pediatrics. Guidelines for the administration of medication in school. *2003;112(3 pt 1):697-9.*
24. Mellins CA, Brackis-Cott E, Dolezal C, Abrams EJ. The role of psychosocial and family factors in adherence to antiretroviral treatment in human immunodeficiency virus-infected children. *Pediatr Infect Dis J* 2004;23:1035-41.
25. Anderson BJ, Vangness L, Connell A, Butler D, Goebel-Fabbri A, Laffel LM. Family conflict, adherence, and glycaemic control in youth with short duration Type 1 diabetes. *Diabet Med* 2002;19:635-42.
26. Penza-Clyve SM, Mansell C, McQuaid EL. Why don't children take their asthma medications? A qualitative analysis of children's perspectives on adherence. *J Asthma* 2004;41:189-97.
27. Macharia WM, Leon G, Rowe BH, Stephenson BJ, Haynes RB. An overview of interventions to improve compliance with appointment keeping for medical services. *JAMA* 1992;267:1813-7.
28. Lieberman DA. Management of chronic pediatric diseases with interactive health games: theory and research findings. *J Ambul Care Manage* 2001;24:26-38.
29. Rapoff MA, Belmont JM, Lindsley CB, Olson NY. Electronically monitored adherence to medications by newly diagnosed patients with juvenile rheumatoid arthritis. *Arthritis Rheum* 2005;48:905-10.