
Family Practice Grand Rounds

Management Problems in Dealing With an Adolescent Diabetic

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DR. ROBERT B. GWINN (*Second-year resident in Family Practice*): Today we will discuss the problem of adherence to a treatment plan in a 21-year-old woman with insulin-dependent diabetes mellitus. There is evidence that good control of serum glucose levels is significant in reducing the sequelae of diabetes.¹ It is also clear that the quality of life at any given time, in terms of sense of well-being and such complications as vaginal candidiasis, can also be improved. Adequate control of diabetes is, therefore, important for both the immediate well-being and the future of the patient. The difficulty in accomplishing this goal has been a source of frustration to many clinicians. Today we shall present a multidisciplinary approach to such a patient.

Our discussion will be presented by the patient's three primary care providers: a physician, a social worker, and a dietitian. We have also asked Peggy Crawford, a nurse clinician from the Endocrine and Metabolic Diseases Unit, to discuss her experiences with her practice group of young diabetics.

At the age of 16 years, this previously healthy woman presented to the Family Practice Center

complaining of vaginal discharge. During the visit, symptoms of polydipsia, polyphagia, and nocturia were elicited. A serum glucose was found to be 532 mg/dL. There were no allergies, and she was taking no medications. A review of symptoms was unremarkable. She was a student in high school living at home with her parents and a younger sister who had a suspected learning disability. Figure 1 displays her family tree.

The patient was admitted to the hospital for control of diabetes mellitus. Physical examination at the time was unremarkable except for erythema and satellite lesions around the external genitalia. Ophthalmologic consultation confirmed no retinopathy. She was discharged on 10 U of isophane purified beef insulin suspension (NPH) and 7 U of regular insulin each day and a 2,400-calorie American Diabetic Association (ADA) diet. She was followed as an outpatient with urine self-testing. Over the next three years, her urine glucose was maintained at 1 to 2+ with an occasional 3+. Her insulin was increased to 15 units of NPH and 5 units of regular insulin each morning and 5 units of NPH in the afternoon. During the next year, she developed four episodes of vaginal candidiasis but no ketoacidosis.

One and one-half years after diagnosis, she developed an abscessed pilonidal cyst, which was treated on an outpatient basis. This treatment was unsuccessful, and she was admitted to the hospital for surgical drainage. A random glucose level after drainage was 490 mg/dL. She was discharged on

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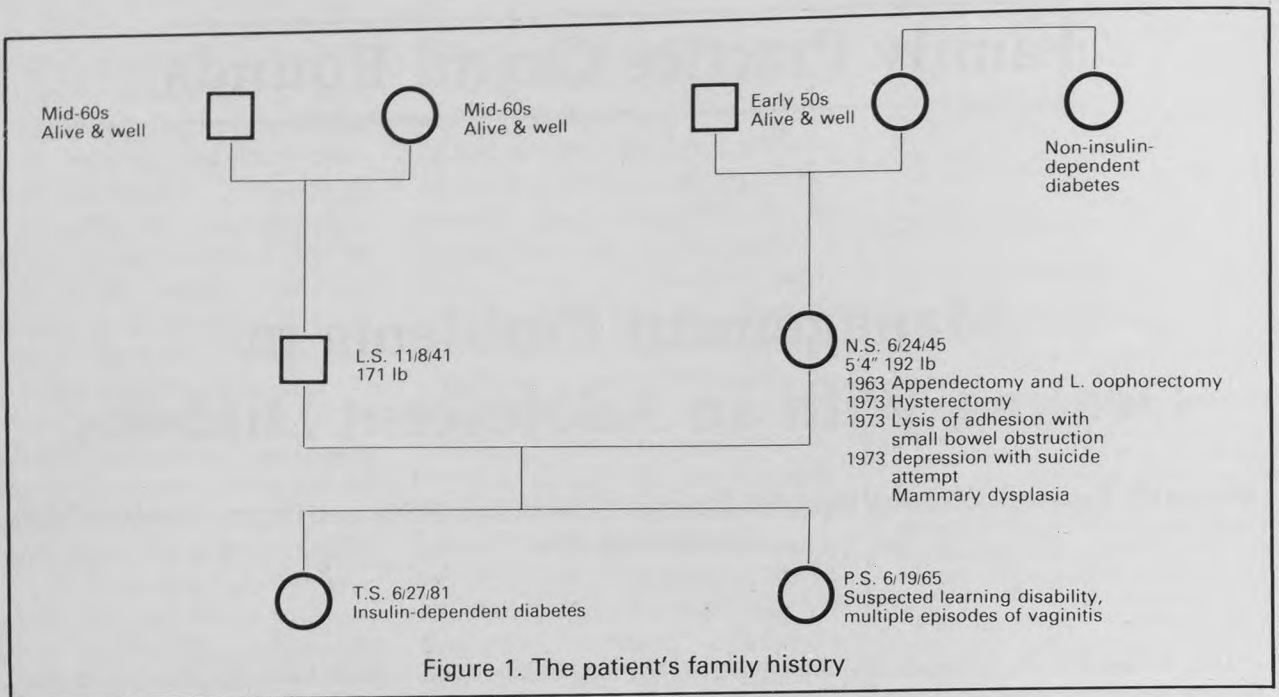


Figure 1. The patient's family history

50 units of NPH and 10 units of regular insulin in the morning and 15 units of regular insulin each afternoon. A 2,100-calorie ADA diet was prescribed. She was 5 ft 7 in tall and weighed 156 lb. At this time her problem list included (1) insulin-dependent diabetes mellitus, (2) poor dietary adherence, (3) dysfunctional family dynamics, and (4) exogenous depression.

After discharge, she began counseling with the Family Practice Center social worker and registered dietitian. Over the next three months adherence was poor. The patient gained 22 lb during this time, and her serum glucose was poorly controlled. As the patient reacted to increases in insulin doses with hostility and depression, the team decided to concentrate more on behavioral changes directed at dietary control than on insulin manipulation. Over the next three months, the patient developed strong ties with all members of our team. She made great strides in her ability to communicate and gained an understanding of the disease and her dietary requirements. She has since maintained a stable weight and reasonably stable glucose and has had no episodes of vaginitis. Her most recent fasting serum glucose was 220 mg/dL and her two-hour postprandial glucose was 293 mg/dL. Attempts are still being made for better adherence and lower glucose levels.

NANCY OLEX (*Registered dietitian, Department of Family Practice*): Dietary counseling involved the use of food records for diet histories, food models for portion size-illustrations, label-reading activities, meal-timing manipulations, emotional support, and acceptance. The diet histories revealed continued excessive intake of simple sugar foods as snacks. The availability of these foods was assured, as the patient's mother did the grocery shopping and bought many sweets for the family. In addition, the patient frequently purchased candy for herself at work. Upon finding a boyfriend who showed interest in helping her manage her diabetes, she became more responsive to her dietary adherence. Over 10 weeks, she steadily lost 5.5 lb and became much more interested in learning about the role of diet in diabetes management. During periods of strife with her boyfriend, the overeating became pronounced and weight gain occurred. Through behavioral and dietary counseling, the patient began to gain insight into the relationship between her emotional state and her dietary intake.

CAROLYN WHITMAN (*Social worker, Department of Family Practice*): The importance of a supportive family in the management of a diabetic adolescent cannot be underestimated. The patient

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we are presenting was not so fortunate, and we believe that her unstable diabetes, depression, and steady weight gain were, in part, brought about by lack of parental support and the family's dysfunction.

According to Teresa, her relationship with her mother had never been satisfactory and had been blighted by her mother's bad temper, physical abuse, occasional bouts of heavy drinking, and involvement with other men. Teresa believed that her mother favored her younger sister, who attended special classes in the public schools.

The parent's relationship was described as poor, with chronic conflict and lack of financial planning and security. The mother frequently accused the father of being an inadequate provider but did very little herself to add to the family finances through either employment or more-prudent management. The father was an understanding, affectionate man, but Teresa recognized his ineffectiveness. He made no effort, apparently, to confront or contain his wife. They functioned poorly as a couple and as parents. Their relationship was characterized by passive-aggressive behavior, generally low compatibility, and rare attempts to resolve issues or problems as they arose.

This family, beleaguered by so many problems, had difficulty accommodating to the additional responsibility of managing a serious health problem. It is for this reason that Teresa preferred the emotional supports offered to her by the health team over the uncertain and reluctant interest of her family. Her wishes not to contact her family were respected.

During her care, Teresa continued to seek her mother's acceptance through appeasement or avoidance, neither of which was conducive to her good health or personal growth. Teresa's tolerance for frustration and rejection was impressive. She was obliged to pay for all her medical expenses, recent hospitalizations, office visits, and medications, even though she was unable to do so. Theresa also paid her tuition and contributed to household costs. Contributing to the cost of foods purchased, however, did not give Teresa any influence over what items were selected at the grocery store. Avoiding favorite foods was difficult for Teresa, as eating was a source of comfort as well as a denial of her diabetes. It was suspected that her lack of dietary adherence supported her fam-

ily's desire to deny her diabetes and maintain its familiar equilibrium. Her preoccupation about the consequences of her diabetes—loss of eyesight or the possibility of amputation—made it increasingly difficult for Teresa to resist food; her consumption increased during her months of depression. Her preoccupation with disease consequences also interfered with her ability to concentrate on studying, leading to failing work at school. Teresa did not rebel against her mother's temper and physical abuse; instead, she felt drawn into concealing her mother's drinking bouts and transient involvements with other men from her father and other family members.

According to research by Greg et al,² the maternal qualities of self-esteem and a sense of personal worth are the chief determinants of a diabetic child's adaptation to his or her disease. Lacking qualities of self-esteem and personal worth, the mother's reaction of guilt by commission or omission will prevail. Without confidence in herself and lacking the support of her husband in the child-rearing, the mother will be unable to model these qualities for her children or carry out the executive function of parenting with her spouse. Without confidence in herself, the mother will have little tolerance for change and be easily threatened by it. This deficit will be marked during a crisis and further strain family relationships. As a result, family function suffers and becomes skewed, in the direction either of enmeshment, permitting little autonomy, or of disengagement, providing little sense of rapport. We observed a similar situation in Teresa's family. Her mother lacked the self-esteem to accept and deal effectively with her daughter's diabetes, and her father was passive with respect to parenting. This situation contributed to the already chaotic state of this family and hence to Teresa's poor adherence to her treatment plan.

Adolescent development imposes such demands on parents. The challenge lies in keeping pace with the young adult's bid for independence while conveying a sense of belonging. Parental understanding and support during this time will lay the groundwork for the adolescent's sense of self-worth and development in initiative.

This family had functioned erratically for years. It is suspected that Teresa kept the family intact on numerous occasions through appeasement of her mother and concealment of her mother's be-

havior, while drawing just enough support from her father to survive. These activities sacrificed her development in the areas of self-confidence and career goal determination. She also lacked strong peer ties and the ability to develop heterosexual relationships. For Teresa, these tasks would have been delayed or abandoned even without the diabetes or without professional support and direction.

Treatment goals were guided by her own emotional needs as she presented them: (1) provide unconditional acceptance, recognition, and patience, (2) improve her relationship with her mother, (3) improve social skills to enhance her friendships with young men, and (4) present alternative career goals.

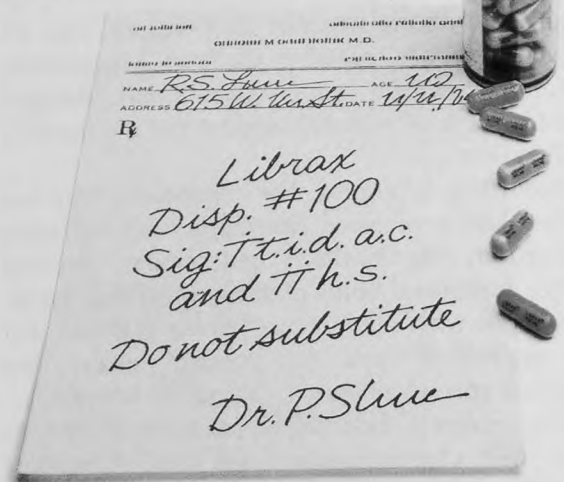
PEGGY CRAWFORD (*Nurse clinician, Diabetes and Endocrine Metabolism Unit*): There are few disorders of childhood that affect the child, his family, his peers, teachers, and health care professionals as does diabetes. The therapeutic procedures focus daily attention upon the details of bodily reactions that, for most of us, go unheeded. All tasks require daily repetition on a schedule that to some extent limits the activity and freedom of the child and his family. Numerous judgments must be made, often on a daily basis, regarding types and amounts of foods, timing of meals and snacks, interpretation of urine results, and doses of insulin.

The procedures are unusual in that they are placed in the hands of the parents and eventually in the hands of the child himself. In a very real sense, we are asking families to become their own providers of health care.

As in other chronic conditions, there are both short-term and long-term goals of treatment. It is crucial to maintain the clinical control of the diabetes at the highest level possible. While the balance among food, insulin, and exercise is critical, so is the balance between ignoring the chronic condition on one hand and making it the focal point of one's entire existence on the other. A second goal, then, is to assist the child and family in developing and maintaining a comfortable attitude toward the condition so that the child can achieve his full potential for social and emotional development. An equally important goal is the shifting of responsibility for care from professionals to parents and child and ultimately to the young adult.

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SPECIFY
LIBRAX®



Each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg clidinium bromide

Please consult complete prescribing information, a summary of which follows:

* **Indications:** Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:
 "Possibly" effective: as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.
 Final classification of the less-than-effective indications requires further investigation.

Contraindications: Glaucoma; prostatic hypertrophy, benign bladder neck obstruction; hypersensitivity to chlordiazepoxide HCl and/or clidinium Br.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants, and against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Physical and psychological dependence rarely reported on recommended doses, but use caution in administering Librium® (chlordiazepoxide HCl/Roche) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions) reported following discontinuation of the drug.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies.

Consider possibility of pregnancy when instituting therapy.

Advise patients to discuss therapy if they intend to or do become pregnant.

As with all anticholinergics, inhibition of lactation may occur.
Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude ataxia, oversedation, confusion (no more than 2 capsules/day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacology of agents, particularly potentiating drugs such as MAO inhibitors, phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions reported in psychiatric patients. Employ usual precautions in treating anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship not established.

Adverse Reactions: No side effects or manifestations not seen with either compound alone reported with Librax. When chlordiazepoxide HCl is used alone, drowsiness, ataxia, confusion may occur, especially in elderly and debilitated; avoidable in most cases by proper dosage adjustment, but also occasionally observed at lower dosage ranges. Syncope reported in a few instances. Also encountered: isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent, generally controlled with dosage reduction; changes in EEG patterns may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice, hepatic dysfunction reported occasionally with chlordiazepoxide HCl, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy, constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

References:

1. Stone PH, Turi ZG, Muller JE: Efficacy of nifedipine therapy for refractory angina pectoris. *Am Heart J* 104:672-681, September 1982.
2. Antman E, Muller J, Goldberg S, et al: Nifedipine therapy for coronary artery spasm: Experience in 127 patients. *N Engl J Med* 302:1269-1273, June 5, 1980.

BRIEF SUMMARY

PROCARDIA* (nifedipine) CAPSULES

For Oral Use

INDICATIONS AND USAGE: I. Vasospastic Angina: PROCARDIA (nifedipine) is indicated for the management of vasospastic angina confirmed by any of the following criteria: 1) classical pattern of angina at rest accompanied by ST segment elevation, 2) angina or coronary artery spasm provoked by ergonovine, or 3) angiographically demonstrated coronary artery spasm. In those patients who have had angiography, the presence of significant fixed obstructive disease is not incompatible with the diagnosis of vasospastic angina, provided that the above criteria are satisfied. PROCARDIA may also be used where the clinical presentation suggests a possible vasospastic component but where vasospasm has not been confirmed, e.g., where pain has a variable threshold on exertion or in unstable angina where electrocardiographic findings are compatible with intermittent vasospasm, or when angina is refractory to nitrates and/or adequate doses of beta blockers.

II. Chronic Stable Angina (Classical Effort-Associated Angina): PROCARDIA is indicated for the management of chronic stable angina (effort-associated angina) without evidence of vasospasm in patients who remain symptomatic despite adequate doses of beta blockers and/or organic nitrates or who cannot tolerate those agents.

In chronic stable angina (effort-associated angina) PROCARDIA has been effective in controlled trials of up to eight weeks duration in reducing angina frequency and increasing exercise tolerance, but confirmation of sustained effectiveness and evaluation of long-term safety in those patients are incomplete.

Controlled studies in small numbers of patients suggest concomitant use of PROCARDIA and beta blocking agents may be beneficial in patients with chronic stable angina, but available information is not sufficient to predict with confidence the effects of concurrent treatment, especially in patients with compromised left ventricular function or cardiac conduction abnormalities. When introducing such concomitant therapy, care must be taken to monitor blood pressure closely since severe hypotension can occur from the combined effects of the drugs. (See Warnings.)

CONTRAINDICATIONS: Known hypersensitivity reaction to PROCARDIA.

WARNINGS: Excessive Hypotension: Although in most patients, the hypotensive effect of PROCARDIA is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension. These responses have usually occurred during initial titration or at the time of subsequent upward dosage adjustment, and may be more likely in patients on concomitant beta blockers.

Severe hypotension and/or increased fluid volume requirements have been reported in patients receiving PROCARDIA together with a beta blocking agent who underwent coronary artery bypass surgery using high dose fentanyl anesthesia. The interaction with high dose fentanyl appears to be due to the combination of PROCARDIA and a beta blocker, but the possibility that it may occur with PROCARDIA alone, with low doses of fentanyl, in other surgical procedures, or with other narcotic analgesics cannot be ruled out. In PROCARDIA treated patients where surgery using high dose fentanyl anesthesia is contemplated, the physician should be aware of these potential problems and, if the patient's condition permits, sufficient time (at least 36 hours) should be allowed for PROCARDIA to be washed out of the body prior to surgery.

Increased Angina: Occasional patients have developed well documented increased frequency, duration or severity of angina on starting PROCARDIA or at the time of dosage increases. The mechanism of this response is not established but could result from decreased coronary perfusion associated with decreased diastolic pressure with increased heart rate, or from increased demand resulting from increased heart rate alone.

Beta Blocker Withdrawal: Patients recently withdrawn from beta blockers may develop a withdrawal syndrome with increased angina, probably related to increased sensitivity to catecholamines. Initiation of PROCARDIA treatment will not prevent this occurrence and might be expected to exacerbate it by provoking reflex catecholamine release. There have been occasional reports of increased angina in a setting of beta blocker withdrawal and PROCARDIA initiation. It is important to taper beta blockers if possible, rather than stopping them abruptly before beginning PROCARDIA.

Congestive Heart Failure: Rarely, patients, usually receiving a beta blocker, have developed heart failure after beginning PROCARDIA. Patients with tight aortic stenosis may be at greater risk for such an event.

PRECAUTIONS: General: Hypotension: Because PROCARDIA decreases peripheral vascular resistance, careful monitoring of blood pressure during the initial administration and titration of PROCARDIA is suggested. Close observation is especially recommended for patients already taking medications that are known to lower blood pressure. (See Warnings.)

Peripheral edema: Mild to moderate peripheral edema, typically associated with arterial vasodilation and not due to left ventricular dysfunction, occurs in about one in ten patients treated with PROCARDIA. This edema occurs primarily in the lower extremities and usually responds to diuretic therapy. With patients whose angina is complicated by congestive heart failure, care should be taken to differentiate this peripheral edema from the effects of increasing left ventricular dysfunction.

Drug Interactions: Beta-adrenergic blocking agents: (See Indications and Warnings.) Experience in over 1400 patients in a non-comparative clinical trial has shown that concomitant administration of PROCARDIA and beta-blocking agents is usually well tolerated, but there have been occasional literature reports suggesting that the combination may increase the likelihood of congestive heart failure, severe hypotension or exacerbation of angina.

Long-acting nitrates: PROCARDIA may be safely co-administered with nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.

Digitalis: Administration of PROCARDIA with digoxin increased digoxin levels in nine of twelve normal volunteers. The average increase was 45%. Another investigator found no increase in digoxin levels in thirteen patients with coronary artery disease. In an uncontrolled study of over two hundred patients with congestive heart failure during which digoxin blood levels were not measured, digitalis toxicity was not observed. Since there have been isolated reports of patients with elevated digoxin levels, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing PROCARDIA to avoid possible over- or under-digitalization.

Carcinogenesis, mutagenesis, impairment of fertility: When given to rats prior to mating, nifedipine caused reduced fertility at a dose approximately 30 times the maximum recommended human dose.

Pregnancy: Category C. Please see full prescribing information with reference to teratogenicity in rats, embryotoxicity in rats, mice and rabbits, and abnormalities in monkeys.

ADVERSE REACTIONS: The most common adverse events include dizziness or light-headedness, peripheral edema, nausea, weakness, headache and flushing each occurring in about 10% of patients, transient hypotension in about 5%, palpitation in about 2% and syncope in about 0.5%. Syncopal episodes did not recur with reduction in the dose of PROCARDIA or concomitant antianginal medication. Additionally, the following have been reported: muscle cramps, nervousness, dyspnea, nasal and chest congestion, diarrhea, constipation, inflammation, joint stiffness, shakiness, sleep disturbances, blurred vision, difficulties in balance, dermatitis, pruritus, urticaria, fever, sweating, chills, and sexual difficulties. Very rarely, introduction of PROCARDIA therapy was associated with an increase in anginal pain, possibly due to associated hypotension.

In addition, more serious adverse events were observed, not readily distinguishable from the natural history of the disease in these patients. It remains possible, however, that some or many of these events were drug related. Myocardial infarction occurred in about 4% of patients and congestive heart failure or pulmonary edema in about 2%. Ventricular arrhythmias or conduction disturbances each occurred in fewer than 0.5% of patients.

Laboratory Tests: Rare, mild to moderate, transient elevations of enzymes such as alkaline phosphatase, CPK, LDH, SGOT, and SGPT have been noted, and a single instance of significantly elevated transaminases and alkaline phosphatase was seen in a patient with a history of gall bladder disease after about eleven months of nifedipine therapy. The relationship to PROCARDIA therapy is uncertain. These laboratory abnormalities have rarely been associated with clinical symptoms. Cholestasis, possibly due to PROCARDIA therapy, has been reported twice in the extensive world literature.

HOW SUPPLIED: Each orange, soft gelatin PROCARDIA CAPSULE contains 10 mg of nifedipine. PROCARDIA CAPSULES are supplied in bottles of 100 (NDC 0069-2600-66), 300 (NDC 0069-2600-72), and unit dose (10x10) (NDC 0069-2600-41). The capsules should be protected from light and moisture and stored at controlled room temperature 59° to 77°F (15° to 25°C) in the manufacturer's original container.

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For young people with diabetes, this assumption of responsibility is a task that extends over a period of many years and requires much patience, cooperation, and support from parents and professionals. Primarily a learning task, this is complicated by the unique fears, anxieties, and attitudes developed around the condition by each child and his family. Success in acquiring independence in self-care depends on many factors, such as readiness on the child's part to take on new responsibility and on the parent's to give it up, ongoing educational programs, and positive consequences to learning. Successful assumption of responsibility often leads to the development of feelings of adequacy and competence of achievement. The young person begins to feel as though he can manage and control the diabetes instead of the diabetes managing and controlling him. It is during this period of adolescence, with its special physiologic changes, social demands, and emphasis on independence, that the impact of diabetes upon developmental progress is probably strongest. It is well known that the adolescent with diabetes has a tendency to experiment with his therapy, to reject his diet, falsify his urine records, and even omit his insulin in an effort to assume control over his own life. This attitude of experimentation, rebellion, or independence is a necessary part of the adolescent development of all young people as they work toward defining their own identity.

Adolescence is a time when periods of poor control seem to occur capriciously, without apparent causes of diet, insulin, or emotional events. It has been suggested that emotional stress, factors associated with maturation, changing exercise patterns, and rebellion against restrictions may contribute to variability in control. Especially during these times of poor control parents are more likely to be aware of the possibility of complications, more aware than are their children, although parental anxiety is easily communicated to the child. The responsibility for maintaining low levels of sugar in the blood and urine is placed in the hands of the child and his parents. With regular monitoring of urine and blood sugar, they are provided concrete evidence and reminders of the success or failure in accomplishing this task. During periods of poor control, parents search anx-

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Azo Gantrisin®
Each tablet contains 0.5 Gm sulfisoxazole/Roche and 50 mg phenazopyridine HCl.

Before prescribing, please consult complete product information, a summary of which follows:

INDICATIONS: Initial treatment of uncomplicated urinary tract infections caused by susceptible strains of *Escherichia coli*, *Klebsiella* species, *Enterobacter* species, *Proteus mirabilis*, *Proteus vulgaris* and *Staphylococcus aureus* when relief of pain, burning or urgency is needed during first 2 days of therapy. Azo Gantrisin treatment not to exceed 2 days. Evidence lacking that sulfisoxazole plus phenazopyridine HCl better than sulfisoxazole alone after 2 days. Treatment beyond 2 days should only be continued with Gantrisin (sulfisoxazole/Roche). (See DOSAGE AND ADMINISTRATION.) *Important Note:* Coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response. With ongoing therapy, add aminobenzoic acid to culture media. Increasing resistance of organisms may limit sulfonamide usefulness. As identical doses produce wide variations, measure blood levels in patients receiving sulfonamides for serious infections: 12 to 15 mg/100 ml is optimal; adverse reactions are more frequent above 20 mg/100 ml.

CONTRAINDICATIONS: Children under 12; known sensitivity to either component; pregnancy at term and during nursing period; in glomerulonephritis, severe hepatitis, uremia and pyelonephritis of pregnancy with gastrointestinal disturbances.

WARNINGS: Sulfonamides are bacteriostatic; organisms causing common infections are often resistant. Sulfas won't eradicate group A streptococci or prevent sequelae like rheumatic fever and glomerulonephritis. Deaths from hypersensitivity reactions, hepatocellular necrosis, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Perform blood counts and renal function tests.

PRECAUTIONS: *General:* Use with caution in patients with impaired renal or hepatic function, severe allergy, bronchial asthma. Hemolysis may occur in glucose-6-phosphate dehydrogenase-deficient individuals.

The more soluble sulfonamides are associated with fewer renal complications. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Information for Patients: Maintain adequate fluid intake; urine will turn reddish-orange.

Laboratory Tests: Perform urinalysis with careful microscopic examination at least once a week and regular blood counts after 2 weeks therapy; measure blood levels in patients with serious infection (see INDICATIONS). *Drug Interactions:* Sulfonamides may displace oral anticoagulants from plasma protein binding sites, increasing anticoagulant effect. Can also displace methotrexate. *Drug Laboratory Test Interactions:* May affect liver function tests in hepatitis.

Carcinogenesis, Mutagenesis, Impairment of Fertility: *Carcinogenesis:* Azo Gantrisin has not undergone adequate trials relating to carcinogenicity; each component, however, has been evaluated separately. Rats appear especially susceptible to goitrogenic effects of sulfonamides; long-term administration has resulted in thyroid malignancies in this species.

Long-term administration of phenazopyridine HCl has induced neoplasia in rats (large intestine) and mice (liver). No association between phenazopyridine HCl and human neoplasia reported; adequate epidemiological studies have not been conducted. *Mutagenesis:* No studies available. *Impairment of Fertility:* The components of Azo Gantrisin have been evaluated in animal reproduction studies. In rats given 800 mg/kg/day sulfisoxazole, there were no effects on mating behavior, conception rate or fertility index. Fertility was not affected in a two-litter study of rats given 50 mg/kg/day phenazopyridine.

Pregnancy: Teratogenic Effects: Pregnancy Category C. The components of Azo Gantrisin have been evaluated. At 800 mg/kg/day sulfisoxazole was nonteratogenic in rats and rabbits, with no perinatal or postnatal effects in rats. In two other studies, cleft palates developed in rats and mice after 500 to 1000 mg/kg/day sulfisoxazole. No congenital malformations developed in rats given 50 mg/kg/day phenazopyridine. As there are no satisfactory animal or human studies, it is not known whether Azo Gantrisin can cause fetal harm or affect reproduction capacity. Use during pregnancy only if the potential benefit justifies the potential risk to the fetus. *Nonteratogenic Effects, Nursing Mothers and Pediatric Use:* See CONTRAINDICATIONS.

ADVERSE REACTIONS: *Allergic:* Anaphylaxis, generalized allergic reactions, angioneurotic edema, arteritis and vasculitis, myocarditis, serum sickness, conjunctival and scleral injection, periarteritis nodosa, systemic lupus erythematosus. *Cardiovascular:* Tachycardia, palpitations, syncope, cyanosis. *Dermatologic:* Rash, urticaria, pruritus, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, photosensitivity. *Endocrine:* Goiter production, diuresis, hypoglycemia. Cross-sensitivity with some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents may exist. *Gastrointestinal:* Nausea, emesis, abdominal pain, anorexia, diarrhea, glossitis, stomatitis, flatulence, salivary gland enlargement, G.I. hemorrhage, pseudomembranous enterocolitis, melena, pancreatitis, hepatic dysfunction, jaundice, hepatocellular necrosis. *Genitourinary:* Crystalluria, hematuria, BUN and creatinine elevation, nephritis and toxic nephrosis with oliguria and anuria, acute renal failure, urinary retention. *Hematologic:* Leukopenia, agranulocytosis, aplastic anemia, thrombocytopenia, purpura, hemolytic anemia, anemia, eosinophilia, clotting disorders including hypoprothrombinemia and hypofibrinogenemia, sulfhemoglobinemia, methemoglobinemia. *Musculoskeletal:* Arthralgia, chest pain, myalgia. *Neurologic:* Headache, dizziness, peripheral neuritis, paresthesia, convulsions, tinnitus, vertigo, ataxia, intracranial hypertension. *Psychiatric:* Psychosis, hallucinations, disorientation, depression, anxiety. *Miscellaneous:* Edema (including periorbital), pyrexia, drowsiness, weakness, fatigue, lassitude, rigors, flushing, hearing loss, insomnia, pneumonitis.

OVERDOSAGE: *Signs:* Anorexia, colic, nausea, vomiting, dizziness, drowsiness, unconsciousness; possibly pyrexia, hematuria, crystalluria. Blood dyscrasias and jaundice may occur later. *Treatment:* Institute gastric lavage or emesis; force oral fluids; administer intravenous fluids if urine output is low with normal renal function. Monitor blood counts and appropriate blood chemistries, including electrolytes. In cyanosis, consider methemoglobinemia and treat with intravenous 1% methylene blue. Institute specific therapy for blood dyscrasias or jaundice.

DOSAGE AND ADMINISTRATION: Azo Gantrisin is intended for the acute, painful phase of urinary tract infections. The recommended dosage in adults is 4 to 6 tablets initially, followed by 2 tablets four times daily for up to 2 days. Treatment with Azo Gantrisin should not exceed 2 days. Treatment beyond 2 days should only be continued with Gantrisin (sulfisoxazole/Roche).

HOW SUPPLIED: Tablets, each containing 0.5 Gm sulfisoxazole/Roche and 50 mg phenazopyridine HCl—bottles of 100 and 500.

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iously for factors that may have contributed to the poor control and, in their haste and anxiety, may blame the child, the physician, or each other unjustly. Friction between parents and teenagers is normal, but it is very difficult to restrict their conflicts to the usual adolescent issues without allowing them to spill over into arguments about diabetes management.

As professionals, we are reasonably well acquainted with *how* adolescent diabetics are non-compliant, but often we are not aware of the various factors contributing to *why*. Sometimes treatment plans are too complicated or too rigid. Diet, for example, is an area of diabetes management with great potential for conflict. Inflexibility in prohibiting certain foods is likely to be disregarded because it overlooks eating and drinking as forms of social intercourse and friendship. Double-voided urine sampling, of debatable value, is an example of the complicated treatment expectations usually ignored by adolescents. Noncompliance can be a way to prove or test one's normality. Many adolescents with diabetes either omit components of their care or ignore symptoms, thereby placing themselves in jeopardy. Adolescents often choose this option in the company of peers for fear they will otherwise be identified as diabetic. Many parents, in fact, have not acknowledged their child's diabetes to others and over the years have encouraged their child also to withhold this information. It is not uncommon for adolescent diabetics to display various risk-taking behaviors such as not eating before physical activity, not carrying any source of sugar for treatment of low blood sugar, or not telling their coach they have diabetes.

Noncompliance with a treatment plan is sometimes related to conflicting, incorrect, or lacking information. For example, the concept of good control is very confusing to professionals, let alone families. To many adolescents and parents alike, good control means avoiding extremes of low blood sugar and diabetic ketoacidosis. Because of this, we often see resistance, especially to changes in the insulin dose, when our goal is to reduce urinary glucose. It is important to remember that many diabetes professionals as well as educational materials expound the virtue of spilling a little sugar in the urine to avoid insulin reactions. Not only is this information incorrect, it

is misleading. Once families have been indoctrinated with information, even incorrect information, it is difficult to alter their behavior.

It is not uncommon to find adolescents who test their urines but then falsify their record, especially when they get high readings. This behavior may be a search for perfection or approval, or it may be an expression of denial, anger, or avoidance of confrontation. Children quickly realize that both professionals and parents prefer low readings to high readings, so they tell us what we want to hear.

Another form of reinforcement for this poor compliance is the way we feed diabetic children in response to their urinary glucose levels. For example, children are given sweets for negative tests but less desired foods for high readings.

Insulin and diet are sometimes deliberately manipulated, resulting in illness and hospitalization. This behavior may reflect attention seeking, dependency needs, school avoidance, or escape from less than adequate living situations.

Adolescents are quite honest about being non-compliant; in fact, many can explain why they are. For example, one older adolescent who rarely tested his urine explained that when he did test and got high readings, he felt obligated to adjust his insulin but hesitated to do so for fear of making the wrong decision. Not testing prevented him from having to make any decision. Feelings of helplessness and frustration often result in the abandonment of the diabetes regimen. When diabetes is out of control and various changes do not bring quick results, adolescents fear that nothing will help their situation, and that, indeed, control is not attainable.

One ingredient in noncompliance seems to be inconsistent health care. Often in large medical settings, care is provided by multiple caretakers, each with his own expectations and treatment approach. Visits are often brief, with little time available for questions or ongoing education about diabetes, certainly not the appropriate environment for developing a trusting relationship between adolescent and caregiver. As we become more familiar with the factors involved in poor compliance among adolescents with diabetes, it seems logical that we could make changes in the way we deliver care to this group.

DR. JACK MEDALIE (*Chairman, Department of Family Medicine, Case Western Reserve University, School of Medicine*): I am concerned that

the family was not treated along with this patient. Would anyone here care to comment on that?

DR. TOM METTE (*Director, Family Practice Residency, Cleveland and Metropolitan General Hospital*): This situation could be viewed as a disruption within the family or, more likely, as a disrupted family that lacks the ability to deal with this disease. I would think it better to involve the whole family in counseling to improve their dealing with the problem.

DR. GWINN: This problem was discussed at length when we began treating the patient. At that time we agreed to respect the patient's wishes not to involve her parents for the time being. This decision was made in light of her financial independence and our belief that she would soon move out of her parents' home. We also felt that involving the patient's mother might lead to conflict before we had gained our patient's trust and confidence, thus impairing our relationship with the patient. Now that the patient has developed more skill in verbalizing her feelings, we expect to start working with the family with her cooperation.

DR. MEDALIE: Dr. Dickman, would you comment on the control of this young woman's diabetes?

DR. ROBERT DICKMAN (*Director, Family Practice Residency, Mount Sinai Hospital*): I would say that given the most recent fasting and two-hour postprandial glucose levels, control is still suboptimal.

DR. GWINN: I agree; we are working for better control. We have made a significant improvement in our relationship with this patient that will allow for better control in the future.

In caring for this patient, we were able to observe the dynamics of her family in relationship to the adaptations she made to her disease. The patient's family of origin both directly and indirectly played a major role in the patient's difficulty with adherence. Directly, the parents had lost interest as the patient's adherence waned, which they demonstrated by maintaining an abundance of simple sugar foods in the home available to the patient. This family is tightly enmeshed around the mother, and there was little opportunity for the patient to develop from adolescence to a point at which she could make a good separation from the family as a mature adult responsible for her own care. The patient and her father formed a dyad

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ALDOMET® (Methyldopa MSD)

Tablets, containing 125, 250, or 500 mg methyldopa; Oral Suspension, containing 250 mg methyldopa per 5 ml and alcohol 1%.

Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis; if previous methyldopa therapy has been associated with liver disorders (see Warnings); hypersensitivity.

Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions. With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between 6 and 12 months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood. At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at 6 and 12 months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstated. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first 3 weeks of therapy, occasionally with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first 2 to 3 months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first 6 to 12 weeks of therapy or whenever an unexplained fever occurs. If fever and abnormalities in liver function tests or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstated in such patients. Rarely, a reversible reduction of the white blood cell count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur. Patients should be followed carefully to detect side reactions or unusual manifestations of drug idiosyncrasy.

Pregnancy and Nursing: Use of any drug in women who are or may become pregnant or intend to nurse requires that anticipated benefits be weighed against possible risks; possibility of fetal injury or injury to a nursing infant cannot be excluded. Methyldopa crosses the placental barrier, appears in cord blood, and appears in breast milk.

Precautions: Should be used with caution in patients with history of previous liver disease or dysfunction (see Warnings). May interfere with measurement of: urinary uric acid by the phosphotungstate method, serum creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, falsely high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. It is important to recognize this phenomenon before a patient with a possible pheochromocytoma is subjected to surgery. Methyldopa is not recommended for patients with pheochromocytoma. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has recurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

Adverse Reactions: *Central nervous system:* Sedation, headache, asthenia or weakness, usually early and transient; dizziness, lightheadedness, symptoms of cerebrovascular insufficiency, paresthesias, parkinsonism, Bell's palsy, decreased mental acuity, involuntary choreoathetotic movements; psychic disturbances, including nightmares and reversible mild psychoses or depression. *Cardiovascular:* Bradycardia, prolonged carotid sinus hypersensitivity, aggravation of angina pectoris. Orthostatic hypotension (decrease daily dosage). Edema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyldopa if edema progresses or signs of heart failure appear) *Gastrointestinal:* Nausea, vomiting, distention, constipation, flatus, diarrhea, colitis, mild dryness of mouth, sore or "black" tongue, pancreatitis, sialadenitis. *Hepatic:* Abnormal liver function tests, jaundice, liver disorders. *Hematologic:* Positive Coombs test, hemolytic anemia. Bone marrow depression, leukopenia, granulocytopenia, thrombocytopenia. Positive tests for antinuclear antibody, LE cells, and rheumatoid factor. *Allergic:* Drug-related fever, lupus-like syndrome, myocarditis. *Dermatologic:* Rash as in eczema or lichenoid eruption; toxic epidermal necrolysis. *Other:* Nasal stuffiness, rise in BUN, breast enlargement, gynecomatia, lactation, hyperprolactinemia, amenorrhea, impotence, decreased libido, mild arthralgia, myalgia.

Note: Initial adult dosage should be limited to 500 mg daily when given with antihypertensives other than thiazides. Tolerance may occur, usually between second and third months of therapy; increased dosage or adding a diuretic frequently restores effective control. Patients with impaired renal function may respond to smaller doses. Syncope in older patients may be related to increased sensitivity and advanced arteriosclerotic vascular disease; this may be avoided by lower doses.

For more detailed information, consult your MSD Representative or see Prescribing Information. Merck Sharp & Dohme, Division of Merck & Co., INC., West Point, PA 19486

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within the family that was submissive to and dominated by the mother's will.

We were impressed by the improvement in this patient as she was encouraged and supported in developing her self-identity. The feeling of being out of control in face of a chronic disease emphasizes the need for involving patients in the control of their disease.

Addendum

Six months following Grand Rounds presentation, the patient had undergone a number of changes. She separated from the boyfriend mentioned in this presentation and within three months married another she had met since. Her most recent fasting serum glucose was 110 mg/dL and a two-hour postprandial glucose was 250 mg/dL. A hemoglobin A_{1c} was 8.30 (upper limit, 8.50). Her insulin dose has been decreased 10 units, and her weight has remained stable. Counseling was begun with her mother and immediate family but was discontinued at their request when the patient left home. Most recently, she became pregnant and was referred to a tertiary center for her obstetric care and constant infusion insulin (insulin pump).

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