Eikenella corrodens Infections

Case report in two adolescent females with IDDM

RON S. NEWFIELD, MD
ILEANA VARGAS, MD
ZILLA HUMA, MD

OBJECTIVE — To alert physicians caring for patients with diabetes to the microorganism *Eikenella corrodens* and to discuss the appropriate preventive and therapeutic measures to take against this potentially morbid opportunistic Gram-negative bacilli.

CASES — We present two cases of extra-oral *E. corrodens* infections in adolescent females with IDDM. The first patient had diabetes of 4 years' duration, which was moderately well controlled. Chronic finger biting resulted in a complex felon that evolved gradually and worsened while the patient received cephalexin orally. Delay in seeking further intervention resulted in necrosis of her distal fingertip and nail bed. The second patient had poorly controlled diabetes for 5 years. She developed an acute thigh abscess at an insulin injection site that resolved after drainage and intravenous antibiotics.

CONCLUSIONS — *E. corrodens* commonly inhabits the human oral cavity and becomes a pathogen mostly when host defenses are impaired, causing abscesses and infections that are at times fatal. Patients with IDDM are compromised hosts and with daily microtrauma to their skin via glucose monitoring and insulin injections, are prone to develop *E. corrodens* infections that can be introduced through oral secretions by licking or biting their skin. Educational efforts aimed at preventing exposure of traumatized skin to oral secretions can minimize the risk of *E. corrodens* infections in compromised hosts. Early intravenous administration of antibiotics, bearing in mind *E. corrodens* resistance to clindamycin, metronidazole, and other antibiotics, coupled with prompt surgical intervention, is essential in successfully managing *E. corrodens* infections.

Eikenella corrodens is a slow-growing facultatively anaerobic Gram-negative bacillus. It is undoubtedly a human pathogen, displaying opportunistic characteristics. Infections in normal hosts have been reported but are infrequent. Most patients with *E. corrodens* infections have reduced host defenses (1–5) due to trauma, surgery, or chronic or debilitating illnesses, such as malignancies, or from receiving immunosuppressive therapy. We present two adolescent patients with IDDM who developed *E. corrodens* infections (apparently the first report in literature in English), where reduced host defenses are attributed to IDDM, the routine microtrauma to the skin associated with insulin injections and blood glucose monitoring, and exposure of broken skin surfaces to oral secretions. Diagnosis of *E. corrodens* infection, its unusual antibiotic sensitivities, and its treatment will be discussed.

CASE REPORT I — A 14-year-old black female with IDDM for 4 years was admitted in moderately good glycemic control, with an HbA_{1c} level of 8.7% (normal, 4.5–6.5%). Over the 9 months preceding her admission, her mean HbA_{1c} was 9.6% (range 8.7–11.3%). She had been chronically biting her fingernails and fingertips. Ten days before her admission, the fingertip of her fourth digit on the right hand gradually became tender, swollen, and erythematous. Four days before her admission, her pediatrician had started her on 500 mg of oral cephalexin, three times daily, along with hot soaks. On follow-up with the pediatrician, she developed pus, bluish discoloration, and decreased range of motion of her distal phalanx.

She was admitted (not in ketoacidosis) with a low-grade fever of 38.6°C. She was immediately sent to the operating room for a wide excision and drainage of a complex felon, and 3 cm^3 of pus was drained. A Gram stain showed Gram-positive cocci in pairs and chains, and cultures from her pus grew many *E. corrodens*, *Enterococcus fecaelis*, and a few coagulase-negative staphylococci. She received two doses of unasyn before switching empirically to nafcillin and clindamycin. *E. corrodens* sensitivities were checked, according to the manual and conventional Kirby Bauer method, and the organism was found to be sensitive to cefazolin, penicillin, ampicillin, and gentamicin. It was resistant to clindamycin, and sensitivity to nafcillin was not reported. Nafcillin was switched to penicillin-G, gentamicin was added for synergy for both organisms, and ampicillin was used a few days later as well. The patient underwent imaging studies of the affected digit, such as magnetic resonance imaging (MRI), bone scan, and labeled indium-111, to rule out osteomyelitis, none of which were conclusive. Despite initial surgery followed by 2 weeks of intravenous antibiotics and daily wound care, she eventually required a second surgical intervention. She underwent debridement of the distal phalangeal tip, which involved removal of the nail and nail bed and resulted in shortening of the digit.

CASE REPORT II — A 13-year-old midpubertal black female with IDDM for 5 years had multiple admissions for poor control due to noncompliance and lack of adequate parental supervision. On admission, her HbA_{1c} level was 10.2%, and over the year preceding her admission, her mean HbA_{1c} was 11.2% (range 9.9–12.5%). She presented at this institution's diabetes clinic with a 2-cm tender lesion

From the Department of Pediatrics, Division of Pediatric Endocrinology, The New York Hospital, Cornell Medical Center, New York, New York.

Address correspondence and reprint requests to Ron S. Newfield, MD, Department of Pediatrics, Rm. N-236, The New York Hospital, Cornell Medical Center, 525 E. 68th St., New York, NY 10021.

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at an insulin injection site on her right anterior thigh, judged to be a hematoma. She was admitted to this institution's Children's Clinical Research Center the next day under an institutionally approved protocol, and informed consent was obtained from her legal guardian. She had a soft tissue infection to her thigh and a raised lesion that was nonfluctuant, tender, warm, and erythematous (7 cm). She was afebrile with no inguinal lymphadenopathy, and her leukocyte count and erythrocyte sedimentation rate were not elevated. Her blood glucose level was 25.9 mmol/l (466 mg/dl), without ketoacidosis. She was started on intravenous nafcillin and gentamicin. After 36 h of intravenous antibiotics, the involved area became larger, and fluctuance was suspected. A sonogram showed a 1.1 × 1.2 cm abscess, and 1.5 cm^3 of brown yellow putrid pus was aspirated. A Gram stain demonstrated Gram-positive cocci in pairs and clusters and also bacilli. Culture grew *E. corrodens* that was sensitive to nafcillin, penicillin, and cephalothin, but resistant to clindamycin. After the drainage, she continued to improve on intravenous nafcillin alone for 10 days and was discharged home on cephalexin, taken orally for an additional week.

CONCLUSIONS— In 1958, Eiken first characterized 21 strains of fastidious Gram-negative anaerobic rods possessing a typical colony morphology that appeared to corrode or pit blood agar surfaces (6). A review by Chen and Wilson (1) of *E. corrodens* in human oral and nonoral infections elaborates on the morphologic, biochemical, serological, and genotypic characteristics of this facultatively anaerobic Gram-negative bacillus. Since Eiken's initial report, which concentrated on abscess isolates from the oral region, there have been many reports of *E. corrodens* infections, both in adults and children. *E. corrodens* is a common inhabitant in the human oral cavity, with only a few clones from this species apparently being pathogenic (1). Therefore, *E. corrodens* infections are often due to orally contaminated wounds (2–4,7,8) associated with fist fights, clenched fists, tooth lacerations, or bites. Extra-oral infections have been described in numerous sites (1–6,9,10), including, among others, brain abscesses, subdural empyema, sinusitis, pneumonia with empyema, osteomyelitis, or endocarditis. Extra-oral infections carry considerable morbidity and, at times, are fatal, especially if the central nervous system is affected. These infections are explained either by bacteria (10,11) or by direct contact with oral or upper respiratory tract secretions, as in aspiration pneumonia. *E. corrodens* is also present in the gastrointestinal and genital tracts themselves, as evident by its isolation in intra-abdominal abscess often related to surgery (2–5,12), or rarely, a Bartholin abscess (13) or intrauterine device infection (14).

In review of the literature, four patients with diabetes were previously reported to develop *E. corrodens* infections, all of whom were adults. The first patient was a 66-year-old female patient with NIDDM, who also had metastatic gastric carcinoma. She developed an abdominal abscess with *E. corrodens* after abdominal surgery (5). The three other patients (type of diabetes unspecified), aged 31, 51, and 52 years old, had subacute or chronic infections to their feet with multiple organisms, and failure of conventional antibiotics to cover *E. corrodens* resulted in osteomyelitis (15).

E. corrodens is mostly a pathogen when host defenses are compromised. Infections are often indolent, but can be acute, with *E. corrodens* isolated alone, but more commonly, in synergy with streptococci, staphylococci, or other organisms. *E. corrodens* abscesses often mimic mixed anaerobic infections with yellow, green, or brown putrid pus. We will now discuss what predisposed our two patients to present with *E. corrodens* infections, and most importantly, how to best treat such infections when they occur, as well as ways to prevent infections with *E. corrodens* in diabetic subjects and other susceptible hosts.

In the adult diabetic population, ischemic changes to the skin, primarily in the feet, due to changes in the micro- and macrovasculature play a major role in susceptibility to infection and poor wound healing. Unlike in adults, peripheral neuropathy does not contribute to the risk of infection in adolescent patients with IDDM. Ineffective phagocytosis, decreased chemotactic activity of polymorphonuclear leukocytes, and serum opsonizing capacity have long been recognized in patients with diabetes of different ages (16) but most likely play a minor role.

In the first patient, chronic finger and nail biting exposed broken skin to oral secretions, which frequently harbor *E. corrodens*. Paronychial infections with *E. corrodens* were reported in healthy children sucking or biting their fingers (17) and may progress to osteomyelitis (18). It is also conceivable that pricking the skin for blood glucose monitoring provided a port of entry.

In our second patient, the infection occurred at an insulin injection site. Good cleansing of the skin before injecting insulin would seem crucial in preventing infection, though evidence to the contrary exists (19,20). Licking an insulin injection site, a wound, or broken skin elsewhere may be a more important factor then previously suspected, and avoiding that practice would prevent exposure to oral secretions and, thus, infections with *E. corrodens* or other oral pathogens.

The mainstays of successful treatment of *E. corrodens* infections are as follows:

1. Suspect *E. corrodens* in any abscess, especially abdominal, oral, or where exposure to oral secretion is possible. In addition, suspect *E. corrodens* in soft tissue infections not responding to routine antibiotics, such as nafcillin or cephalothin. Note that a Gram stain showing Gram-negative bacilli is an important tip-off. The microbiology lab should be instructed to look for this fastidious organism, retaining routine aerobic cultures for 48 h longer or growing this organism in 5–10% CO_2.

2. Suspecting *E. corrodens* should direct antibiotic coverage before sensitivities, knowing it is universally resistant to clindamycin and metronidazole (1–3) (drugs commonly used in abscesses due to anaerobes). Brooks et al. (2) documented partial resistance to methicillin and cephalothin in vitro and reported on patients who developed *E. corrodens* infections while receiving those drugs. Our first patient did not respond to oral cephalexin, in spite of organism sensitivity to it in vitro. Similar findings were reported (15), with resistance to nafcillin, oxacillin, dicloxacillin, and cephalexin, in adult patients with diabetes; treatment with those antibiotics resulted in indolent chronic infections of the patients' feet and progression to osteomyelitis. Some *E. corrodens* strains are also relatively resistant to aminoglycosides. Recommendations for antibiotic coverage vary. Ampicillin

and penicillin are generally recommended (1–4,12), although strains not responding to penicillin were reported (21,22). *E. corrodens* is uniformly sensitive to tetracycline and chloramphenicol (1–4), which are used in patients with drug allergies. Goldstein and colleagues (23,24) have found that *E. corrodens* is not uniformly sensitive to all the new β-lactams, second and third generations cephalosporins. Overall, *E. corrodens* showed good susceptibility to commonly used antibiotics, such as cefoxitin, cefotetan, cefotaxime, ceftriaxone, ticarcillin, and moxalactam. For empirical treatment of diabetic subjects' feet infections, some recommend using cefoxitin or imipenem (15).

3. Early surgical drainage, when indicated, together with appropriate antibiotics coverage is of the utmost importance in treating *E. corrodens* infections successfully (2,3).

Our two cases underscore the need to educate patients with IDDM and their parents about the dangers associated with licking their wounds or fingertips after blood glucose monitoring. In addition, we advocate for aggressive and early institution of intravenous antibiotics in any soft tissue infection in patients with diabetes. We are hopeful that increased awareness to *E. corrodens* will raise the index of suspicion and thus contribute to optimal management of these infections, minimizing the significant morbidity associated with this organism.

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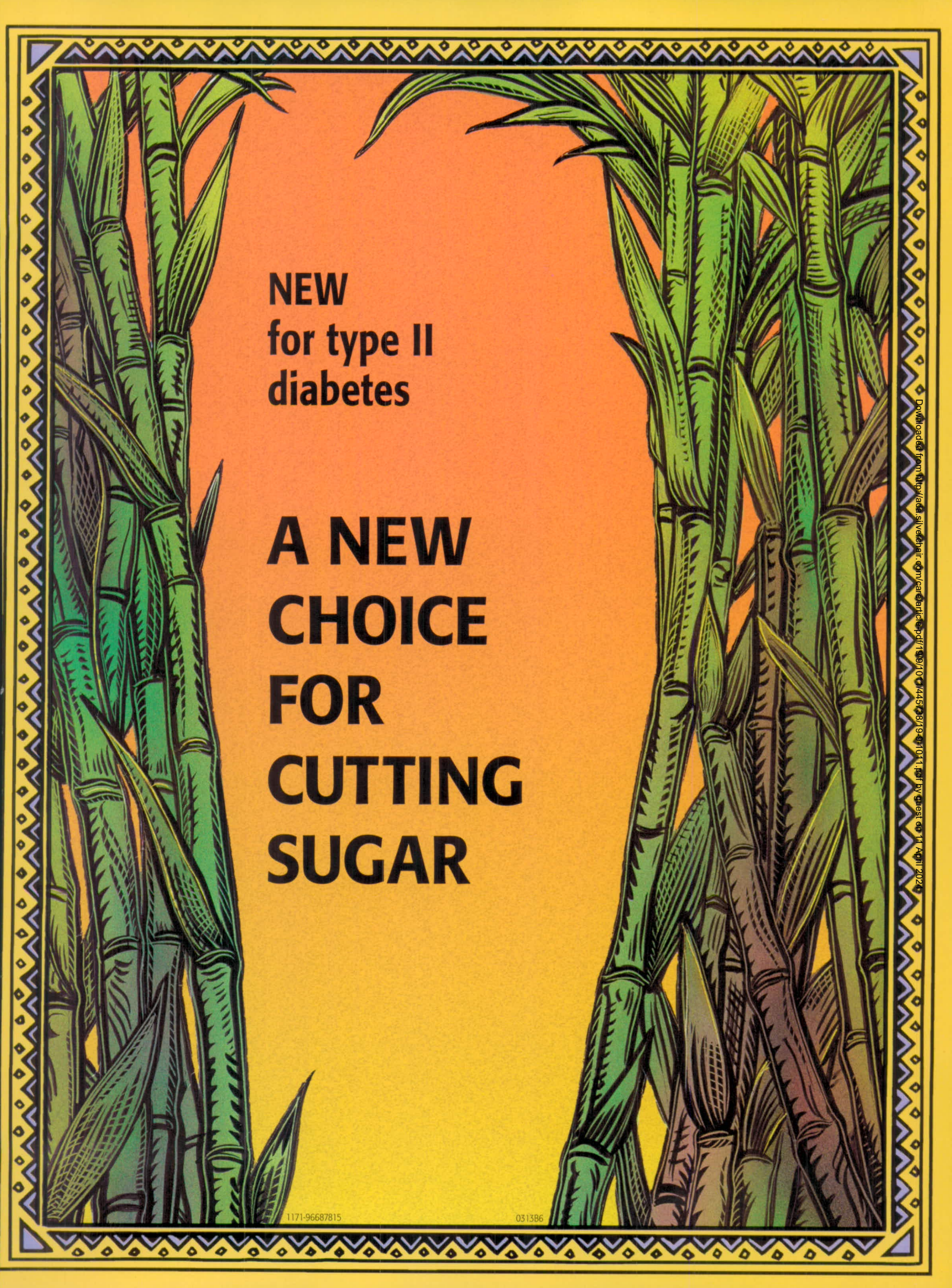

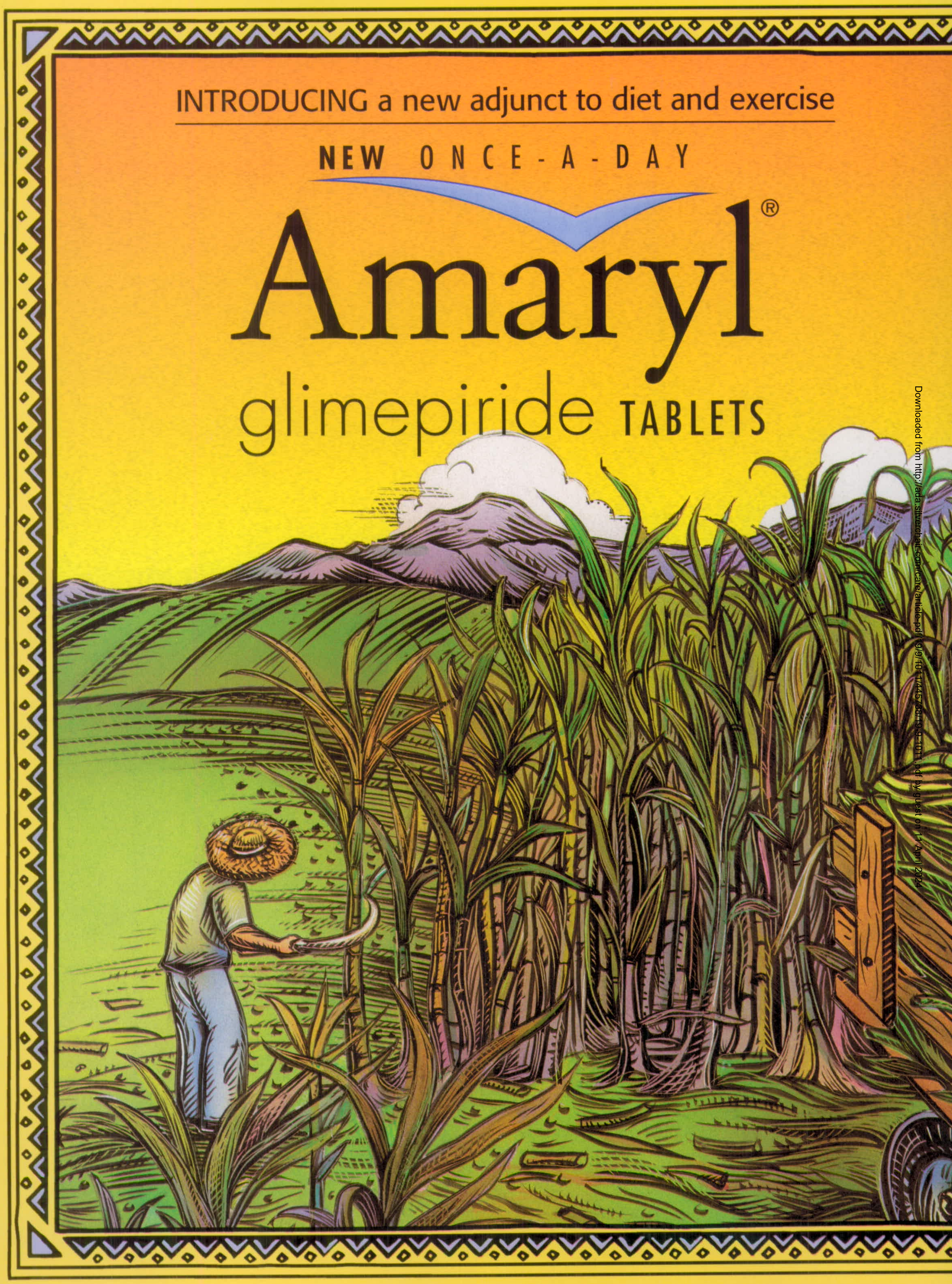

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Brief Summary

Drug Interactions

The hypoglycemic action of sulfonylureas may be potentiated by certain drugs, including nonsteroidal anti-inflammatory drugs and other drugs that are highly protein bound, such as salicylates, sulfonamides, chloramphenicol, coumarins, probenecid, monoamine oxidase inhibitors, and beta adrenergic blocking agents.

Certain drugs tend to produce hyperglycemia and may lead to loss of control. These drugs include the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, and isoniazid.

A potential interaction between oral miconazole and oral hypoglycemic agents leading to severe hypoglycemia has been reported. Whether this interaction also occurs with the intravenous, topical, or vaginal preparations of miconazole is not known. Potential interactions of glimepiride with other drugs metabolized by cytochrome P450 II C9 also include phenytoin, diclofenac, ibuprofen, naproxen, and mefenamic acid.

Although no specific interaction studies were performed, pooled data from clinical trials showed no evidence of clinically significant adverse interactions with uncontrolled concurrent administration of calcium-channel blockers, estrogens, fibrates, NSAIDs, HMG CoA reductase inhibitors, sulfonamides, or thyroid hormone.

INDICATIONS AND USAGE

AMARYL is indicated as an adjunct to diet and exercise to lower the blood glucose in patients with noninsulin-dependent (Type II) diabetes mellitus (NIDDM) whose hyperglycemia cannot be controlled by diet and exercise alone.

AMARYL is also indicated for use in combination with insulin to lower blood glucose in patients whose hyperglycemia cannot be controlled by diet and exercise in conjunction with an oral hypoglycemic agent. Combined use of glimepiride and insulin may increase the potential for hypoglycemia.

CONTRAINDICATIONS

AMARYL is contraindicated in patients with

1. Known hypersensitivity to the drug.
2. Diabetic ketoacidosis, with or without coma. This condition should be treated with insulin.

WARNINGS

SPECIAL WARNING ON INCREASED RISK OF CARDIOVASCULAR MORTALITY

The administration of oral hypoglycemic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin.

PRECAUTIONS

General

Hypoglycemia: All sulfonylurea drugs are capable of producing severe hypoglycemia. Patients with impaired renal function may be more sensitive to the glucose-lowering effect of AMARYL. A starting dose of 1 mg once daily followed by appropriate dose titration is recommended in those patients. Debilitated or malnourished patients, and those with adrenal, pituitary, or hepatic insufficiency are particularly susceptible to the hypoglycemic action of glucose-lowering drugs. Hypoglycemia is more likely to occur when caloric intake is deficient, after severe or prolonged exercise, when alcohol is ingested, or when more than one glucose-lowering drug is used.

Loss of control of blood glucose: When a patient stabilized on any diabetic regimen is exposed to stress such as fever, trauma, infection, or surgery, a loss of control may occur. At such times, it may be necessary to add insulin in combination with AMARYL or even use insulin monotherapy. Should secondary failure occur with AMARYL monotherapy, AMARYL-insulin combination therapy may be instituted. Combined use of glimepiride and insulin may increase the potential for hypoglycemia.

Information for Patients

Patients should be informed of the potential risks and advantages of AMARYL and of alternative modes of therapy. They should also be informed about the importance of adherence to dietary instructions, of a regular exercise program, and of regular testing of blood glucose.

The risks of hypoglycemia, its symptoms and treatment, and conditions that predispose to its development should be explained to patients and responsible family members. The potential for primary and secondary failure should also be explained.

Laboratory Tests

Fasting blood glucose should be monitored periodically to determine therapeutic response. Glycosylated hemoglobin should also be monitored, usually every 3 to 6 months, to more precisely assess long-term glycemic control.

Carcinogenesis, Mutagenesis, and Impairment of Fertility

Studies in rats at doses of up to 5000 ppm in complete feed (approximately 340 times the maximum recommended human dose, based on surface area) for 30 months showed no evidence of carcinogenesis. In mice, administration of glimepiride for 24 months resulted in an increase in benign pancreatic adenoma formation which was dose related and is thought to be the result of chronic pancreatic stimulation. The no-effect dose for adenoma formation in mice in this study was 320 ppm in complete feed, or 46-54 mg/kg body weight/day. This is about 35 times the maximum human recommended dose of 8 mg once daily based on surface area.

Glimepiride was non-mutagenic in a battery of in vitro and in vivo mutagenicity studies (Ames test, somatic cell mutation, chromosomal aberration, unscheduled DNA synthesis, mouse micronucleus test).

There was no effect of glimepiride on male mouse fertility in animals exposed up to 2500 mg/kg body weight (>1,700 times the maximum recommended human dose based on surface area). Glimepiride had no effect on the fertility of male and female rats administered up to 4000 mg/kg body weight (approximately 4,000 times the maximum recommended human dose based on surface area).

Pregnancy

Teratogenic Effects

Pregnancy Category C. Glimepiride did not produce teratogenic effects in rats exposed orally up to 4000 mg/kg body weight (approximately 4,000 times the maximum recommended human dose based on surface area) or in rabbits exposed up to 32 mg/kg body weight (approximately 60 times the maximum recommended human dose based on surface area). Glimepiride has been shown to be associated with intrauterine fetal death in rats when given in doses as low as 50 times the human dose based on surface area and in rabbits when given in doses as low as 0.1 times the human dose based on surface area. This fetotoxicity, observed only at doses inducing maternal hypoglycemia, has been similarly noted with other sulfonylureas, and is believed to be directly related to the pharmacologic (hypoglycemic) action of glimepiride.

There are no adequate and well-controlled studies in pregnant women. On the basis of results from animal studies, AMARYL should not be used during pregnancy. Many experts recommend that insulin be used during pregnancy to maintain glucose levels as close to normal as possible.

Nonteratogenic Effects

In some studies in rats, offspring of dams exposed to high levels of glimepiride during pregnancy and lactation developed skeletal deformities consisting of shortening, thickening, and bending of the humerus during the postnatal period. Significant concentrations of glimepiride were observed in the serum and breast milk of the dams as well as in the serum of the pups. These skeletal deformations were determined to be the result of nursing from mothers exposed to glimepiride.

Prolonged severe hypoglycemia (4 to 10 days) has been reported in neonates born to mothers who were receiving a sulfonylurea drug at the time of delivery. This has been reported more frequently with the use of agents with prolonged half-lives. Patients who are planning a pregnancy should consult their physician, and it is recommended that they change over to insulin for the entire course of pregnancy and lactation.

Nursing Mothers

In rat reproduction studies, significant concentrations of glimepiride were observed in the serum and breast milk of the dams, as well as in the serum of the pups. Although it is not known whether AMARYL is excreted in human milk, other sulfonylureas are excreted in human milk. AMARYL should be discontinued in nursing mothers. If AMARYL is discontinued, and if diet and exercise alone are inadequate for controlling blood glucose, insulin therapy should be considered. (See above ***Pregnancy, Nonteratogenic Effects***)

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

The incidence of hypoglycemia with AMARYL, as documented by blood glucose values <60 mg/dL, ranged from 0.9-1.7% in two large, well-controlled, 1-year studies. (See **WARNINGS** and **PRECAUTIONS**)

AMARYL has been evaluated for safety in 2,013 patients in US controlled trials, and in 1,551 patients in foreign controlled trials. More than 1,650 of these patients were treated for at least 1 year.

Adverse events, other than hypoglycemia, considered to be possibly or probably related to study drug that occurred in US placebo-controlled trials in more than 1% of patients treated with AMARYL are shown below.

Adverse Events Occurring in ≥1% AMARYL Patients

	AMARYL		Placebo	
	No.	%	No.	%
Total Treated	746	100	294	100
Dizziness	13	1.7	1	0.3
Asthenia	12	1.6	3	1.0
Headache	11	1.5	4	1.4
Nausea	8	1.1	0	0.0

Gastrointestinal Reactions

Vomiting, gastrointestinal pain, and diarrhea have been reported, but the incidence in placebo-controlled trials was less than 1%. Isolated transaminase elevations have been reported. Cholestatic jaundice has been reported to occur rarely with sulfonylureas.

Dermatologic Reactions

Allergic skin reactions, e.g., pruritus, erythema, urticaria, and morbilliform or maculopapular eruptions, occur in less than 1% of treated patients. These may be transient and may disappear despite continued use of AMARYL; if skin reactions persist, the drug should be discontinued. Porphyria cutanea tarda and photosensitivity reactions have been reported with sulfonylureas.

Hematologic Reactions

Leukopenia, agranulocytosis, thrombocytopenia, hemolytic anemia, aplastic anemia, and pancytopenia have been reported with sulfonylureas.

Metabolic Reactions

Hepatic porphyria reactions and disulfiram-like reactions have been reported with sulfonylureas; however, no cases have yet been reported with AMARYL. Cases of hyponatremia have been reported with glimepiride and all other sulfonylureas, most often in patients who are on other medications or have medical conditions known to cause hyponatremia or increase release of antidiuretic hormone. The syndrome of inappropriate antidiuretic hormone (SIADH) secretion has been reported with certain other sulfonylureas, and it has been suggested that these sulfonylureas may augment the peripheral (antidiuretic) action of ADH and/or increase release of ADH.

Other Reactions

Changes in accommodation and/or blurred vision may occur with the use of AMARYL. This is thought to be due to changes in blood glucose, and may be more pronounced when treatment is initiated. This condition is also seen in untreated diabetic patients, and may actually be reduced by treatment. In placebo-controlled trials of AMARYL, the incidence of blurred vision was placebo, 0.7%, and AMARYL, 0.4%.

OVERDOSAGE

Overdosage can produce hypoglycemia. Mild hypoglycemic symptoms without loss of consciousness or neurologic findings should be treated aggressively with oral glucose and adjustments in drug dosage and/or meal patterns. Close monitoring should continue until the physician is assured that the patient is out of danger. Severe hypoglycemic reactions with coma, seizure, or other neurological impairment occur infrequently, but constitute medical emergencies requiring immediate hospitalization. If hypoglycemic coma is diagnosed or suspected, the patient should be given a rapid intravenous injection of concentrated (50%) glucose solution. This should be followed by a continuous infusion of a more dilute (10%) glucose solution at a rate that will maintain the blood glucose at a level above 100 mg/dL. Patients should be closely monitored for a minimum of 24 to 48 hours, because hypoglycemia may recur after apparent clinical recovery.

DOSAGE AND ADMINISTRATION

There is no fixed dosage regimen for the management of diabetes mellitus with AMARYL or any other hypoglycemic agent.

Usual Starting Dose

The usual starting dose of AMARYL as initial therapy is 1-2 mg once daily, administered with breakfast or the first main meal. Those patients who may be more sensitive to hypoglycemic drugs should be started at 1 mg once daily, and should be titrated carefully. (See **PRECAUTIONS** Section for patients at increased risk).

No exact dosage relationship exists between AMARYL and the other oral hypoglycemic agents. The maximum starting dose of AMARYL should be no more than 2 mg.

Failure to follow an appropriate dosage regimen may precipitate hypoglycemia. Patients who do not adhere to their prescribed dietary and drug regimen are more prone to exhibit unsatisfactory response to therapy.

Usual Maintenance Dose

The usual maintenance dose is 1 to 4 mg once daily. The maximum recommended dose is 8 mg once daily. After reaching a dose of 2 mg, dosage increases should be made in increments of no more than 2 mg at 1-2 week intervals based upon the patient's blood glucose response. Long-term efficacy should be monitored by measurement of HbA1c levels, for example, every 3 to 6 months.

AMARYL®-Insulin Combination Therapy

Combination therapy with AMARYL and insulin may be used in secondary failure patients. The fasting glucose level for instituting combination therapy is in the range of >150 mg/dL in plasma or serum depending on the patient. The recommended AMARYL dose is 8 mg once daily administered with the first main meal. After starting with low-dose insulin, upward adjustments of insulin can be done approximately weekly as guided by frequent measurements of fasting blood glucose. Once stable, combination-therapy patients should monitor their capillary blood glucose on an ongoing basis, preferably daily. Periodic adjustments of insulin may also be necessary during maintenance as guided by glucose and HbA1c levels.

Specific Patient Populations

AMARYL is not recommended for use in pregnancy, nursing mothers, or children. In elderly, debilitated, or malnourished patients, or in patients with renal or hepatic insufficiency, the initial dosing, dose increments, and maintenance dosage should be conservative to avoid hypoglycemic reactions (See **PRECAUTIONS**, ***General***).

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References: 1. Kramer W, Müller G, Girbig F, et al. Differential interaction of glimepiride and glibenclamide with the β-cell sulfonylurea receptor: II. photoaffinity labeling of a 65 kDa protein by [^{3}H]glimepiride. *Biochim Biophys Acta.* 1994;1191:278-290. 2. Müller G, Hartz D, Pünter J, Ökonomopulos R, Kramer W. Differential interaction of glimepiride and glibenclamide with the β-cell sulfonylurea receptor: I. binding characteristics. *Biochim Biophys Acta.* 1994; 1191:267-277. 3. Data on file, Hoechst Marion Roussel.

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Agenda:

Scope of the Problem
Maureen I. Harris, Ph.D., MPH;
Susceptibility of Complications: Ethnic and Racial Variations
Lewis H. Kuller, MD, DrPH
Prevention of Complications in the Management of IDDM: Blood Glucose Control
Robert A. Rizza, MD
Diagnosis and Management of Diabetic Dyslipidemia
Frederick L. Dunn, MD
Nephropathy in NIDDM
Michael W. Steffes, MD, Ph.D.
Diagnosis and Classification of Neuropathy
Eva L. Feldman, MD, Ph.D.
Treatment of Neuropathy
Douglas A. Greene, MD
Agenda Strategies to Prevent Lower Extremity Amputations
Lee J. Sanders, DPM
Treatment of Coronary Artery Disease
Richard W. Nesto, MD
The Role of Primary Care Physicians in the Detection of Retinopathy
Frederick L. Ferris III, MD
Future Therapies in Diabetes Care
Jay S. Skyler, MD

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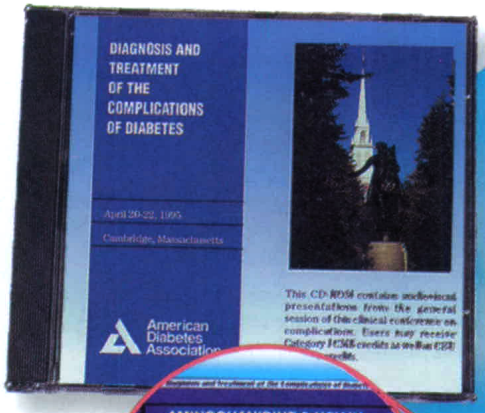

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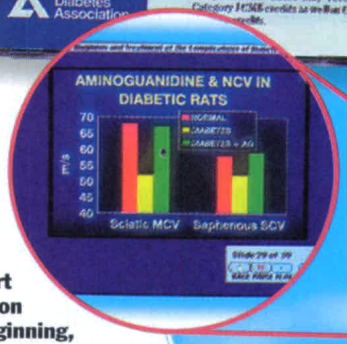

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