The Journal of the American Diabetes Association

diabetes

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CONTENTS

ORIGINAL CONTRIBUTIONS

ADENOSINE TRIPHOSPHATE LEVELS OF MAMMALIAN PANCREATIC B CELLS AFTER STIMULATION WITH GLUCOSE AND HYPOGLYCEMIC SULFONYLUREAS 509
Bo Hellman, M.D., Lars-Ake Idahl, M.K., and Ake Danielsson, M.K., Umea, Sweden

POTENTIATION OF THE PLASMA INSULIN RESPONSE TO GLUCOSE BY PRIOR ADMINISTRATION OF ALCOHOL 517
An Apparent Islet-priming Effect
Robert Metz, M.B., Ph.D., Sheldon Berger, M.D., and Mary Mako, M.S., Chicago, Illinois

EFFECT OF PROTEIN MEALS ON PLASMA INSULIN IN MILDLY DIABETIC PATIENTS 523
Stefan S. Fajans, M.D., John C. Floyd, Jr., M.D., Sumer Pek, M.D., Ralph F. Knopf, M.D., Mitchell Jacobson, M.D., and Jerome W. Conn, M.D., Ann Arbor, Michigan

BIOLOGICAL ACTIVITIES OF TOLBUTAMIDE AND ITS METABOLITES 529
A Dissociation of Insulin-releasing and Hypoglycemic Activity
Jerome M. Feldman, M.D., and Harold E. Lebovitz, M.D., Durham, North Carolina

POSSIBLE ROLE OF HYDRAZINE GROUP IN HYPOGLYCEMIA ASSOCIATED WITH THE USE OF CERTAIN MONOAMINE-OXIDASE INHIBITORS (MAOI's) 538
William Z. Potter, M.S., Daniel S. Zaharko, Ph.D., and Lyle V. Beck, Ph.D., Bloomington, Indiana

RESISTANCE OF RABBITS AND GUINEA PIGS TO THE DIABETOGENIC EFFECT OF STREPTOZOTOCIN 542
B. Kushner, B.S., M. Lazar, M.D., M. Furman, M.S., T. W. Lieberman, M.D., and I. H. Leopold, M.D., New York, New York

EFFECT OF INSULIN ON THE CONVERSION OF GLUCOSE-C-14 TO C-14-O_2 BY NORMAL AND DIABETIC FIBROBLASTS IN CULTURE 545
Samuel Goldstein, M.D., and John W. Littlefield, M.D., Boston, Massachusetts

EARLY INSULIN SYNERGISTIC ACTIVITY OF GROWTH HORMONE 550
Richard J. Mahler, M.D., and Olga Szabo, B.S., New York, New York

LIPID CLASS AND FATTY ACID COMPOSITION OF RAT BRAIN AND SCIATIC NERVE IN ALLOXAN DIABETES 556
J. Howard Pratt, M.D., James F. Berry, Ph.D., Beverly Kaye, B.S., and Frederick C. Goetz, M.D., Minneapolis, Minnesota

POST-HEPARIN LIPOLYTIC ACTIVITY IN DIABETIC PATIENTS WITH A HISTORY OF MIXED HYPERLIPEMIA 562
Relative Rates Against Artificial Substrates and Human Chylomicrons
Dana E. Wilson, M.D., Paul H. Schreibman, M.D., and Ronald A. Arky, M.D., Boston, Massachusetts

ESTIMATION OF VASCULAR BASEMENT MEMBRANE THICKNESS 567
Theoretical and Practical Considerations
Joseph R. Williamson, M.D., Nancy J. Vogler, B.S., and Charles Kilo, M.D., St. Louis, Missouri

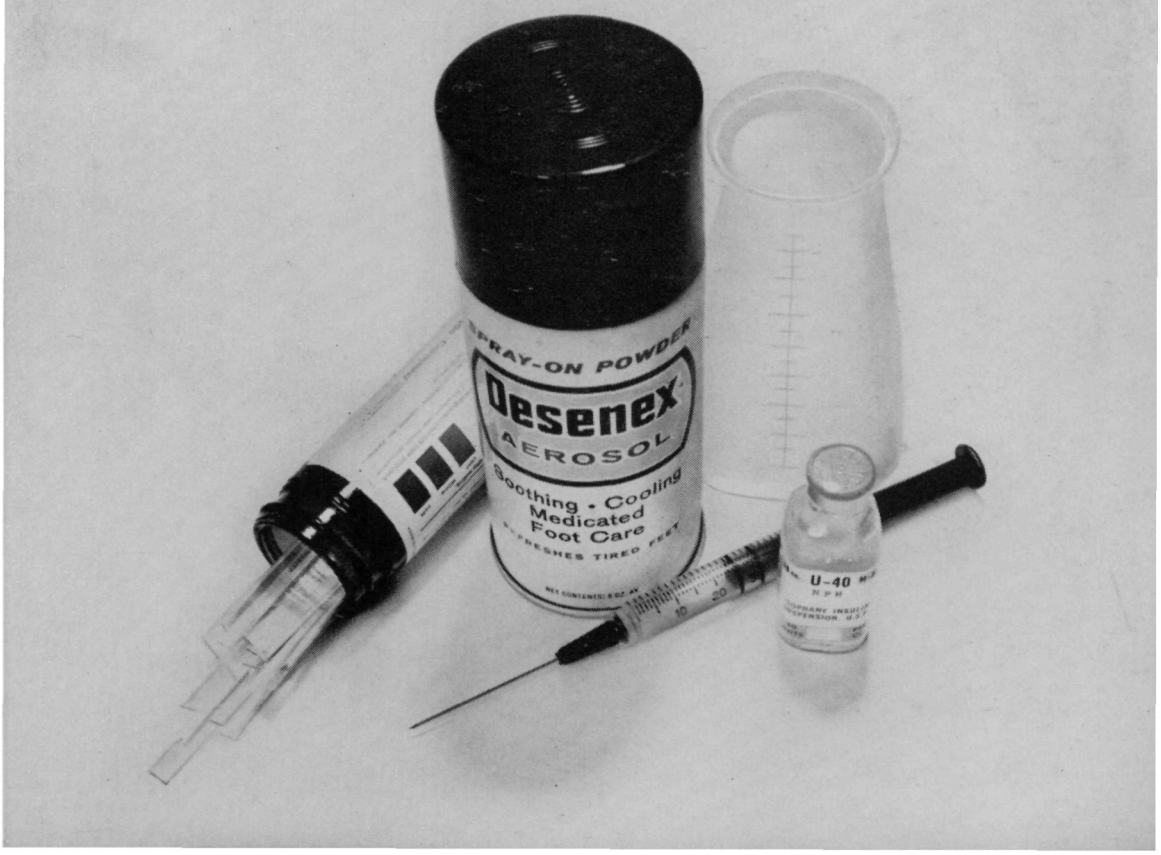
ABSTRACTS 579

ORGANIZATION SECTION 586

NEWS NOTES 588

EIGHTH RESEARCH SYMPOSIUM
September 19-20

Protection with Desenex® helps keep your diabetic patients on their feet.



Patients with peripheral vascular disease or diabetes present a critical foot care problem. Any foot infection can be extremely serious in this group. Fungal infection is always a threat.

DESENEX® Powder or Aerosol soothes the foot, absorbs perspiration, and provides comfort that your diabetic patients appreciate. Even more important, the prophylactic use of DESENEX helps protect against potentially serious fungal foot infection. Used routinely, DESENEX guards against, and helps treat Athlete's Foot. DESENEX is both antifungal and antibacterial. It is medicated with undecylenic acid, a standard Athlete's Foot treatment used by the U. S. Armed Forces.

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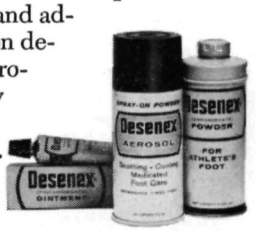

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DIABETES®

The Journal of the American Diabetes Association

DIABETES is published by the American Diabetes Association, Inc., to provide an official Journal for the Association and to furnish the medical profession with information concerning diabetes and related fields of medicine.

Contributions are invited from practicing physicians, clinical and laboratory investigators, and others who have data of importance to offer in these fields. Manuscripts, if suitable, will be accepted providing that the text has not been printed elsewhere.

The Editors will be pleased to consider for publication papers presented at the Annual Meeting of the American Diabetes Association.

Manuscript Specifications: The length of manuscripts (not including special articles or letters) should be limited to 5,000 words, exclusive of illustrations, etc. Exceptions to this limitation may be made at the discretion of the Editors.

Communications for the "Brief Notes and Comments" department should not exceed 1,000 words except in unusual circumstances. Figures and tables in these brief communications should be limited to one of each, and references should not exceed twenty in number.

Manuscripts should be typewritten, with double spacing and, if possible, submitted in triplicate together with three copies of figures and photomicrographs.

References should be presented in the style illustrated by the following examples:

For Periodicals—Banting, F. G., and Best, C. H.: The internal secretion of the pancreas. J. Lab. Clin. Med. 7:251-66, Feb. 1922.

For Books—Allen, Frederick M.: Studies Concerning Glycosuria and Diabetes. Cambridge, Harvard University Press, 1913, p. 461.

An abstract or summary of the content of the paper in not more than 250 words should usually appear at the beginning. If possible, this should be self-contained and understandable without reference to the text.

Photographs, drawings, and figures should be suitable for reproduction purposes. Photographs should be unmounted, untrimmed glossy prints. The names of authors should appear on the back. The tops of photographs and figures should be indicated.

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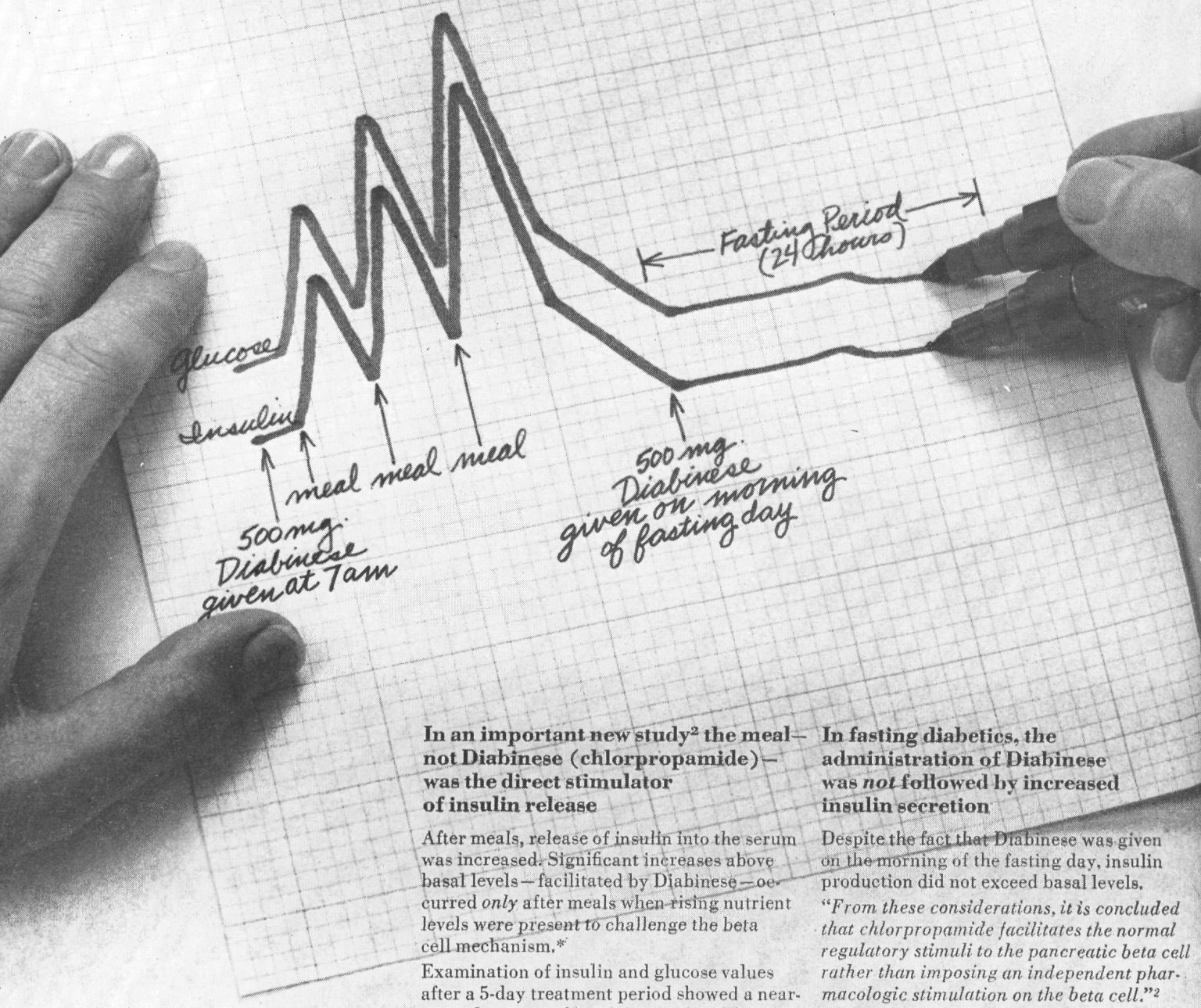
How close can your diabetic patients get to metabolic normalcy?



In an important new study[2] the meal—not Diabinese (chlorpropamide)—was the direct stimulator of insulin release

After meals, release of insulin into the serum was increased. Significant increases above basal levels—facilitated by Diabinese—occurred *only* after meals when rising nutrient levels were present to challenge the beta cell mechanism.*

Examination of insulin and glucose values after a 5-day treatment period showed a near-normal pattern of insulin secretion. That is, the plasma insulin curve very closely paralleled the plasma glucose curve.

In fasting diabetics, the administration of Diabinese was *not* followed by increased insulin secretion

Despite the fact that Diabinese was given on the morning of the fasting day, insulin production did not exceed basal levels.

"From these considerations, it is concluded that chlorpropamide facilitates the normal regulatory stimuli to the pancreatic beta cell rather than imposing an independent pharmacologic stimulation on the beta cell."[2]

*These data do not indicate that hypoglycemia does not occur with Diabinese. As with all sulfonylureas, it may occur when dosage is not properly adjusted to the patient's requirements.

(Chart adapted from Chu, P-C. et al.[2])

It is known that insulin is lipogenic. But increased lipogenesis because of treatment with Diabinese is highly unlikely. In patients receiving the same caloric intake, the insulin output after five weeks of treatment was substantially the same as during the control periods.[2] Of equal importance is the finding that significant increases in insulin secretion beyond basal levels do not occur without glucose challenge during treatment with a sulfonylurea.[2] This limits the likelihood of hypoglycemia during periods of no food intake, providing therapy is tailored to specific patient needs.*

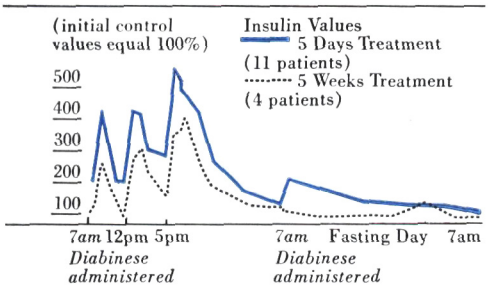
No insulin-induced weight gain

"Objections to the use of sulfonylureas have included a concern for the lipogenic effects, especially in the obese patient, which has not been warranted by the clinical experience of most practitioners."[3]

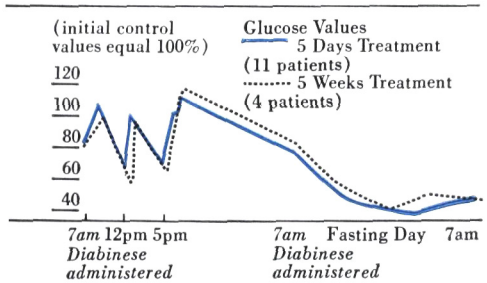
In their study Chu et al.[2] found that the production of insulin in their patients returned to pretreatment levels after initial control was established. Moreover, "After 5 weeks the level of insulin for any given blood glucose value was lower than after 5 days."[2]

Lee[4] also speaks of a return of insulin to pretreatment levels after the first few weeks of therapy, and Reaven and Dray[5] reported that "Plasma insulin did not increase when blood glucose was lowered

5 WEEK INSULIN LEVELS SIGNIFICANTLY LOWER AT ALL TIME POINTS



5 DAY AND 5 WEEK GLUCOSE VALUES SIMILAR



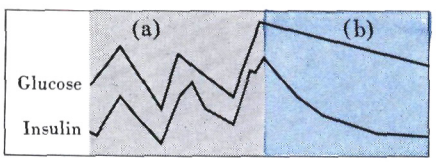
with a sulfonylurea compound, but appeared to decrease." The rarity of insulin-induced lipogenesis with these agents is further borne out by studies in which weight was recorded before and after therapy.[3,6]

(Above illustrative material is adapted from Chu, P-C. et al.[2])

Near-normal carbohydrate metabolism means a closer-to-normal diabetic life

Hypoglycemia unlikely*

Unlike exogenous insulin, sulfonylureas merely facilitate the body's own insulin regulatory mechanism. During the absorptive part of the day, with dosage properly adjusted to patient's requirements, a significant increase in insulin release over basal levels occurs only with rising glucose levels. This is shown in the way the plasma insulin curve closely parallels the plasma glucose curve after meals (fig. a).



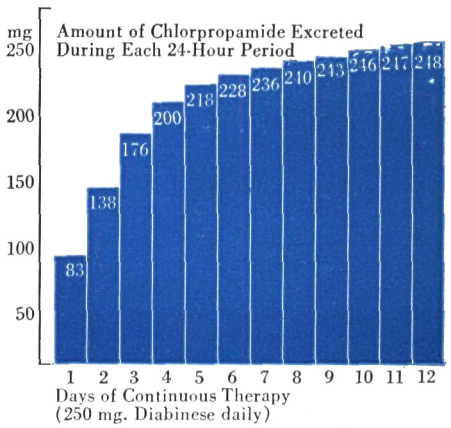
During the night, in the absence of a rise in glucose levels, there is no increase in insulin production (fig. b).

Chlorpropamide concentrations reach a plateau after about 5-7 days of therapy when intake and renal excretion are in balance. In one study[7] blood levels, taken at random in 20 patients who were maintained for one to 20 weeks with 500 mg. Diabinese, ranged within the narrow spectrum of 16 to 20 mg. % after the first week of treatment. In another study[8] involving 60 diabetic patients treated with Diabinese over a period of 8 months, the investigator concluded "There is no accumulation of the drug after long periods of therapy."

Once this characteristic plateau is reached, there is no further accumulation in the blood, provided dosage remains constant, and there is no impairment of renal excretion because of disease or interaction with other drugs.

After about 5-7 days—equilibrium of Diabinese intake and excretion

The half-life of chlorpropamide is 36 hours. Approximately one third of the total amount of the drug in the body is excreted within each 24-hour period. Thus, within a matter of days the intake of chlorpropamide is balanced by the amount excreted. The diagram below is a theoretical construction illustrating how this balance is achieved.



The reality of physiological safeguards against hypoglycemia is best demonstrated by the comparative rarity of this adverse effect in actual practice. Out of 3,749 patients treated, only 58 cases were reported in the 24 studies in English presenting appropriate data and published between January 1962 and December 1967. Of the total, a few patients experienced hypoglycemia sufficiently serious to require discontinuance of therapy.*

*While the incidence of hypoglycemia with oral agents is rare, in some instances it can be severe, depending upon the physiologic status of the patient and the pharmacologic properties of the drug used.

For more detailed information regarding dosage, contraindications, warnings, precautions and adverse effects, refer to Brief Summary on last page of this ad.

start with **Diabinese®** (chlorpropamide)

start with

Diabinese®
(chlorpropamide)

makes good the promise of a closer-to-normal carbohydrate metabolism

With control that facilitates normal regulatory stimuli

With better control initially and over the long term

With more extended long-term control

With control on as little as 100 mg./day for the elderly

With true once-a-day dosage, low-cost control

Contraindications: Diabinese is not indicated as the sole agent in juvenile diabetes, severe or unstable brittle diabetes, and diabetes complicated by ketosis, acidosis, coma, surgery, infections, severe trauma, severe diarrhea, or nausea and vomiting. It is contraindicated in patients with serious impairment of hepatic, renal or thyroid function, and during pregnancy. Serious consideration should attend its use in women of childbearing age. It should be used with caution in patients with Addison's disease and those receiving barbiturates or ingesting alcohol. Consult package insert for further information. Uncooperative or careless patients should not receive Diabinese therapy.

Warnings: Prescription refills should be controlled by the physician. Urine tests for sugar and acetone three times daily and complete weekly medical evaluations are recommended during the first six weeks of therapy. Frequent liver function tests should be seriously considered. *Increasing serum alkaline phosphatase levels may indicate incipient jaundice and the drug should be withdrawn.*

In infection, severe trauma or surgical procedures, it may be necessary to withdraw, temporarily, chlorpropamide therapy and administer insulin alone or insulin and Diabinese.

Precautions: Hypoglycemia may occur. It is usually readily controlled by administration of glucose. Because of the prolonged hypoglycemic action of chlorpropamide, these patients require close observation for at least 3 to 5 days, discontinuance of medication, frequent feedings and glucose administration.

Caution should be exercised when antibacterial sulfonamides, phenylbutazone and oxyphenbutazone, salicylates, probenecid, bishydroxycoumarin, or MAO inhibitors are administered concomitantly with chlorpropamide as hypoglycemia resultant from either potentiation or accumulation of sulfonylureas has been reported.

Chlorpropamide-Phenformin: Dosage of phenformin should be reduced at the first sign of gastrointestinal disturbance. Lactic acidosis and ketonuria without hyperglycemia have been reported with phenformin therapy (see phenformin package insert for complete details).

Adverse Reactions: Usually dose-related and respond to reduction or withdrawal of therapy. Generally transient and not of a serious nature and include anorexia, nausea, vomiting and gastrointestinal intolerance; weakness and paresthesias.

Rare cases of phototoxic reaction have been reported.

Certain untoward reactions associated with idiosyncrasy or hypersensitivity have occasionally occurred. These reactions, which may include jaundice (rarely associated with severe diarrhea and bleeding), skin eruptions rarely progressing to erythema multiforme and exfoliative dermatitis, and probably depression of formed elements of the blood, show no direct relationship to the size of the dose. They occur characteristically during the first six weeks of therapy. With a few exceptions, these manifestations have been mild and readily reversible on the discontinuance of the drug.

The jaundice is cholangiolitic and results primarily from intracanalicular biliary stasis rather than hepatocellular degeneration.

Leukopenia, thrombocytopenia and mild anemia, which occur occasionally, are generally benign and revert to normal, following cessation of the drug. Rare cases of aplastic anemia and agranulocytosis, generally similar to blood dyscrasias associated with other sulfonylureas, have been reported.

As with other sulfonylureas, some side effects associated with hypersensitivity may be severe and death has been reported in rare instances.

Supply: 100 mg. and 250 mg., blue, 'D'-shaped, scored tablets.

More detailed professional information available on request.

References: **1.** Lacy, P. E.: New Eng. J. Med. 276:187, Jan. 26, 1967. **2.** Chu, P.-C., Conway, M. J., Krouse, H. A. and Goodner, C. J.: Ann. Intern. Med. 68:757, Apr., 1968. **3.** Bowers, C. Y. and Hawley, W. D.: Geriatrics 23:146, June, 1968. **4.** Lee, C. T.: Med. Sci. 17:56, Apr., 1966. **5.** Reaven, G. and Dray, J.: Abstract of paper presented at Ann. Meet. A.D.A., Diabetes 14:463, July, 1965. **6.** Skillman, T. A. et al.: Geriatrics 16:209, May, 1961. **7.** Hamwi, G. J. et al.: Ann. N. Y. Acad. Sci. 74:1003, Mar. 30, 1959. **8.** Beaser, S. B.: Ann. N. Y. Acad. Sci. 74:701, Mar. 30, 1959. **9.** Dunlop, D.: St. Bartholomew's Hosp. J.: 67:159, July, 1963. **10.** Moss, J. M. et al.: Scientific Exhibit, A.M.A. Ann. Meet., San Francisco, June 21-25, 1964. **11.** Katz, H. M. and Bissel, G.: Diabetes 14:650, Oct., 1965. **12.** Krall, L. P.: Med. Clin. N. Amer. 45:823, July, 1961. **13.** Parker, A. M.: J. Amer. Geriat. Soc. 11:250, Mar., 1963. **14.** Beaser, S. B.: Paper presented at Ann. Meet., Minn. Acad. Gen. Pract., Minneapolis, Minn., Sept. 29-30, 1965. **15.** Fineberg, S. K.: J. Amer. Geriat. Soc. 14:463, May, 1966.

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MEAL PLANNING PUBLICATIONS AVAILABLE

"Adaptations of Food Exchange Lists for ADA Fat-Controlled Diabetic Diets" and "Diabetic Diet Card for Physicians and Dietitians for Use with Fat-Controlled Diets" have been recently published by The American Dietetic Association in collaboration with the American Diabetes Association and the National Center for Chronic Disease Control of the Public Health Service. The new material may be obtained at the same price as the other individual meal plans and the "Diabetic Diet Card for Physicians": $.05 per single copy; $2.00 per 100 copies; $18.00 per 1,000 copies.

Previously published meal plans also available are Meal Plans No. 1 through No. 9: (1) 1200, (2) 1500, (3) 1800, (4) 2200, (5) 1800, (6) 2600, (7) 3500, (8) 2600, and (9) 3000 calories, respectively. Meal Plans 5, 6 and 7 are especially suitable for children since they contain more milk than the others. "ADA Bland Low-fiber Diabetic Diet"; and "ADA Sodium Restricted Diabetic Diet" also may be obtained. They and the Meal Plans are to be used in conjunction with the Meal Planning Booklet.

The twenty-four page booklet, *Meal Planning with Exchange Lists,* was prepared to help diabetics select foods for their meals. It is available at $.15 each; $6.50 per 100 copies and $50.00 for 1,000 copies.

All costs include handling and shipping.

Order forms for this material are available on request from the offices of the American Diabetes Association, 18 East 48th Street, New York, N. Y. 10017.

the goal was achieved

IN MATURITY-ONSET, NONKETOTIC DIABETICS...

COMPARABLE IN POTENCY TO CHLORPROPAMIDE

COMPARABLE IN SAFETY TO TOLBUTAMIDE

250 MG. TABLETS

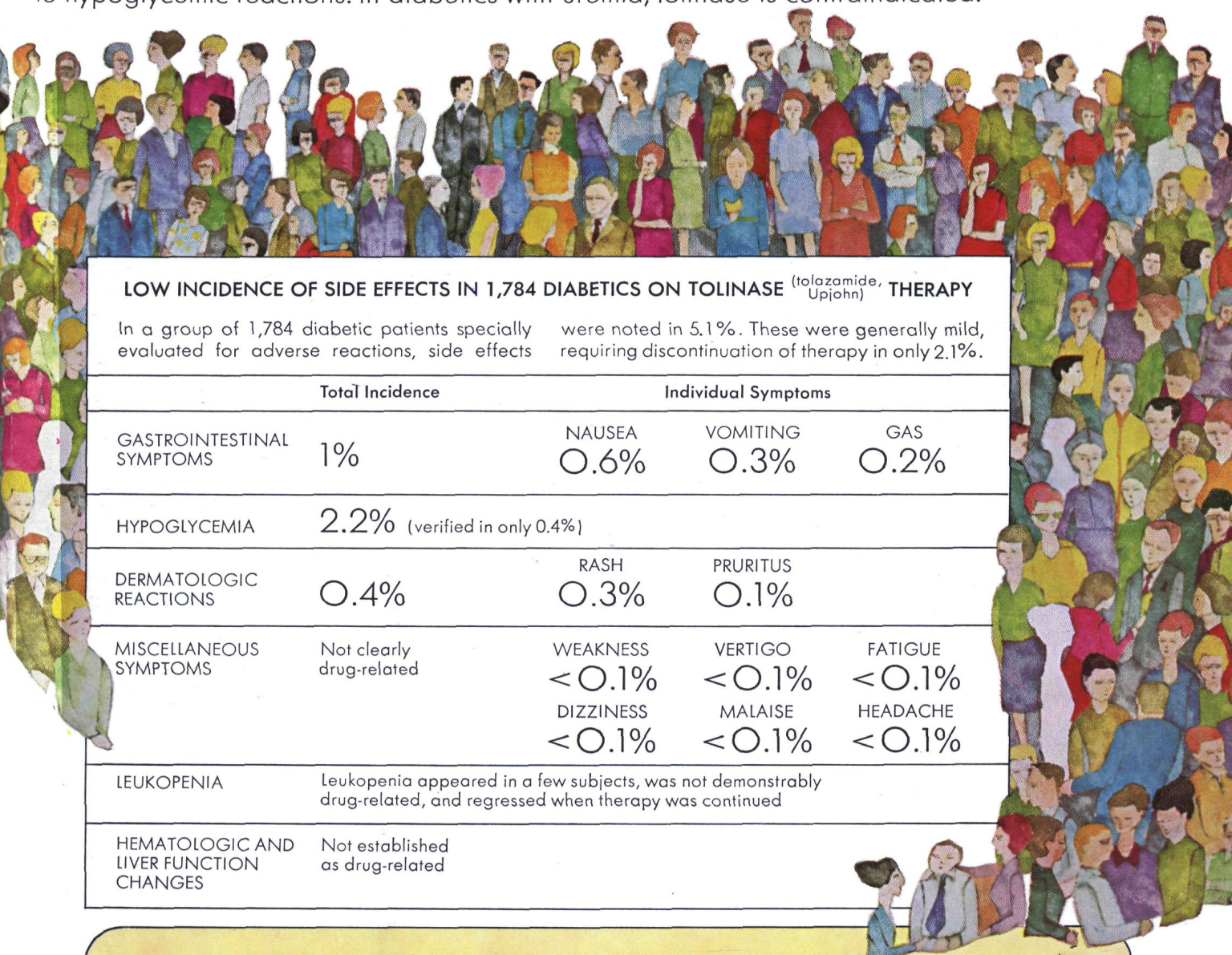
Tolinase®

tolazamide, Upjohn

the safety story

The record for tolbutamide safety is of an unequaled eleven-year duration. However, the three-year experience with Tolinase (tolazamide, Upjohn) shows a *similar low incidence of side effects and toxicity* —and is now of sufficient duration to be considered a probable pattern.

No renal, hematologic, endocrine, or other serious disturbances attributable solely to therapy with Tolinase have been reported. Like all sulfonylureas, Tolinase is not recommended for patients with chronic liver or kidney diseases, as they may well metabolize or excrete the drug poorly, and be more susceptible to hypoglycemic reactions. In diabetics with uremia, Tolinase is contraindicated.



LOW INCIDENCE OF SIDE EFFECTS IN 1,784 DIABETICS ON TOLINASE (tolazamide, Upjohn) THERAPY

In a group of 1,784 diabetic patients specially evaluated for adverse reactions, side effects were noted in 5.1%. These were generally mild, requiring discontinuation of therapy in only 2.1%.

	Total Incidence	Individual Symptoms		
GASTROINTESTINAL SYMPTOMS	1%	NAUSEA 0.6%	VOMITING 0.3%	GAS 0.2%
HYPOGLYCEMIA	2.2% (verified in only 0.4%)			
DERMATOLOGIC REACTIONS	0.4%	RASH 0.3%	PRURITUS 0.1%	
MISCELLANEOUS SYMPTOMS	Not clearly drug-related	WEAKNESS <0.1%	VERTIGO <0.1%	FATIGUE <0.1%
		DIZZINESS <0.1%	MALAISE <0.1%	HEADACHE <0.1%
LEUKOPENIA	Leukopenia appeared in a few subjects, was not demonstrably drug-related, and regressed when therapy was continued			
HEMATOLOGIC AND LIVER FUNCTION CHANGES	Not established as drug-related			

INTRINSIC HYPOGLYCEMIC POTENCY OF TOLINASE (tolazamide, Upjohn) HELPS PROVIDE MORNING-TO-MORNING CONTROL—WITH COMFORT AND CONVENIENCE FOR YOUR PATIENT

Effectiveness: Without gross or troublesome disturbances of a normal sense of well-being

Potency: Intrinsic hypoglycemic potency without prolonged clearance

Safety: Appears to have a low incidence of side effects at all dosage levels

Convenience: One low daily dose (250 mg.) usually sufficient for control

Flexibility: Extended range of usable potency, up to 1,000 mg. daily as needed

JA69-8777

Please see last page of this advertisement for further prescribing information.

IN MATURITY-ONSET DIABETICS

250 MG. TABLETS

Tolinase® tolazamide, Upjohn

An oral hypoglycemic agent effective in the mild to moderately severe maturity onset type of diabetes. Approximately one third of failures to other sulfonylureas or to phenformin will respond to Tolinase (tolazamide), although some of these patients will also eventually fail. Nonresponsive drug failures may respond to combined Tolinase–phenformin therapy. Some patients developing significant side effects or intolerance to other oral drugs may be successfully maintained on Tolinase.
As some diabetics are not suitable candidates for management with Tolinase, it is essential that physicians familiarize themselves with the indications, limits of application, and criteria for selection of patients for this therapy as described in the package insert. Tolinase is not an oral insulin or insulin substitute.

CONTRAINDICATIONS: Tolinase is not indicated in diabetic patients who: are undergoing surgery; have infections or severe trauma; have ketosis, acidosis or coma, or history of repeated bouts of acidosis and coma; or have juvenile or labile (brittle) diabetes. Tolinase is not recommended in patients with concurrent liver, renal, or endocrine disease and is contraindicated in uremia. Safety and usefulness during pregnancy have not been established; therefore Tolinase (tolazamide) is not recommended in the pregnant diabetic patient. Serious consideration should be given to the potential hazards in women who might become pregnant.

PRECAUTIONS: Patients must be under continuous medical supervision particularly during the first six weeks of therapy. They should check their urines daily for sugar and acetone and should see their doctors at least once a week. Diagnostic and therapeutic measures necessary for optimal control with insulin and other sulfonylureas are also necessary with Tolinase. The patient must receive complete instructions: about the nature of his disease; how to prevent and detect complications; how to control his condition; not to neglect dietary restrictions or develop a careless attitude regarding instructions relative to body weight, exercise, and personal hygiene; to avoid infections; how to recognize and counteract impending hypoglycemia; and how and when to test for glycosuria and ketonuria.
Caution, close observation, and careful adjustment of dose are necessary: when insulin is withdrawn during the trial period where the appearance of acidosis, ketosis, or coma would make the discontinuation of Tolinase (tolazamide) and return to insulin therapy mandatory; when Tolinase is administered as sole therapy to patients previously receiving combination therapy; during the transition period from chlorpropamide, to avoid overlapping drug effect and possible hypoglycemia; in administering thiazide type diuretics which may aggravate diabetes; and in debilitated, malnourished, semistarved patients or those not eating properly who may develop severe hypoglycemic reactions requiring corrective therapy. Severe hypoglycemia, though uncommon, may occur and may mimic acute neurologic disorders. Certain conditions such as hepatic and renal disease, malnutrition, debility, advanced age, alcoholism, and adrenal and pituitary insufficiency may predispose to hypoglycemia. Certain drugs such as insulin, phenformin, sulfonamides, oxyphenbutazone, phenylbutazone, salicylates, probenecid, and monamine oxidase inhibitors may increase the risk of hypoglycemia.
When combination therapy with phenformin is elected, the physician should familiarize himself with the prescribing information for that drug.

ADVERSE REACTIONS: Side effects, which were generally mild, occurred in 5.1% of a specially evaluated group of diabetic subjects necessitating discontinuation of therapy in 2.1%. Hypoglycemia was observed in 2.2% and verified by low blood sugar in 0.4% and therapy was discontinued because of hypoglycemia in only 0.5%. Reduction of dose usually results in alleviation of mild to moderately severe hypoglycemic symptoms. Gastrointestinal symptoms such as nausea, vomiting, and gas, and dermatologic symptoms such as rash and pruritus were reported less frequently. Miscellaneous symptoms such as weakness, fatigue, dizziness, vertigo, malaise, and headache were reported infrequently, and the relationship to Tolinase therapy is difficult to assess.
No clinical jaundice, renal, hematologic, endocrine, or other serious disturbance attributable solely to therapy with Tolinase was noted during clinical trials. Side effects have not been shown to be related to size of dose or duration of therapy.
Transient elevations of alkaline phosphatase are not uncommon in initiating sulfonylurea therapy, but may not be necessarily drug related.
Although not demonstrated to be drug related, leukopenia was noted in a few subjects. False-positive urinary albumin tests and disulfiram flushes have not been reported with Tolinase, but have occurred occasionally with other sulfonylureas, and should be kept in mind.

SUPPLIED: *100 mg.* Scored Tablets—bottles of 50. *250 mg.* Scored Tablets—bottles of 50 and cartons of 100 tablets in foil strips.
For additional product information, see package insert or consult your Upjohn representative.

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KALAMAZOO
MICHIGAN 49001

Upjohn

MED B-2-S (KRM-6)

Your patient's chances of keeping this loading dose down are better than 250,000 to 1.

Straight glucose solutions are cloyingly sweet and have a high osmotic pressure; they commonly cause nausea, vomiting and stomach distension. According to a three-year diabetic screening study[1-3], GLUCOLA® avoids these side effects. The glucose in GLUCOLA is partially polymerized so that the sweetness is 40% that of glucose and the osmotic pressure is ¼ that of 100 Gm. of glucose in 7-oz. solution. Result: GLUCOLA tastes good; stays down too! The 7-oz. bottle of GLUCOLA yields 75 Gm. of glucose. When patients take GLUCOLA instead of eating a regular meal, in one- or two-hour blood-glucose testing, you are sure that the glucose challenge is adequate. And when GLUCOLA is used in full-scale glucose tolerance testing, the poor patient acceptance often encountered with unpolymerized glucose preparations is avoided.

References: (1) Leonards, J. R., McCullagh, E. P. and Christopher, T. C.: Diabetes *14*:96 (Feb.) 1965. (2) Leonards, J. R.: Personal Communication. (3) Kent, G. T. and Leonards, J. R.: Diabetes *17*:274 (May) 1968.

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Diabetes Mellitus: Diagnosis and Treatment (Volumes I and II) makes available the current thinking of a large number of authorities on the principal problems associated with diabetes mellitus. The practicing physician will find these volumes convenient reference manuals. Short chapters, each of which deals concisely with a single topic, and the broad scope of the subject matter also make them useful as texts or reference books for teachers, students, interns or residents.

The volumes are units in a series undertaken by the Committee on Professional Education of the American Diabetes Association. They constitute an unusual departure in medical publishing.

Volume II—published in 1967—supplements but does not supplant Volume I—published in mid-1964.

Volume II—with 250 pages and contributions by forty-seven authors, extends the scope of the subject matter covered by 209-page Volume I, to which forty-one authors contributed.

Diabetes Mellitus: Diagnosis and Treatment is published in the spirit of true service to the interested professions and ultimately to the diabetic patient. Hence the Association makes the volumes available at low cost which it hopes will insure their wide distribution.

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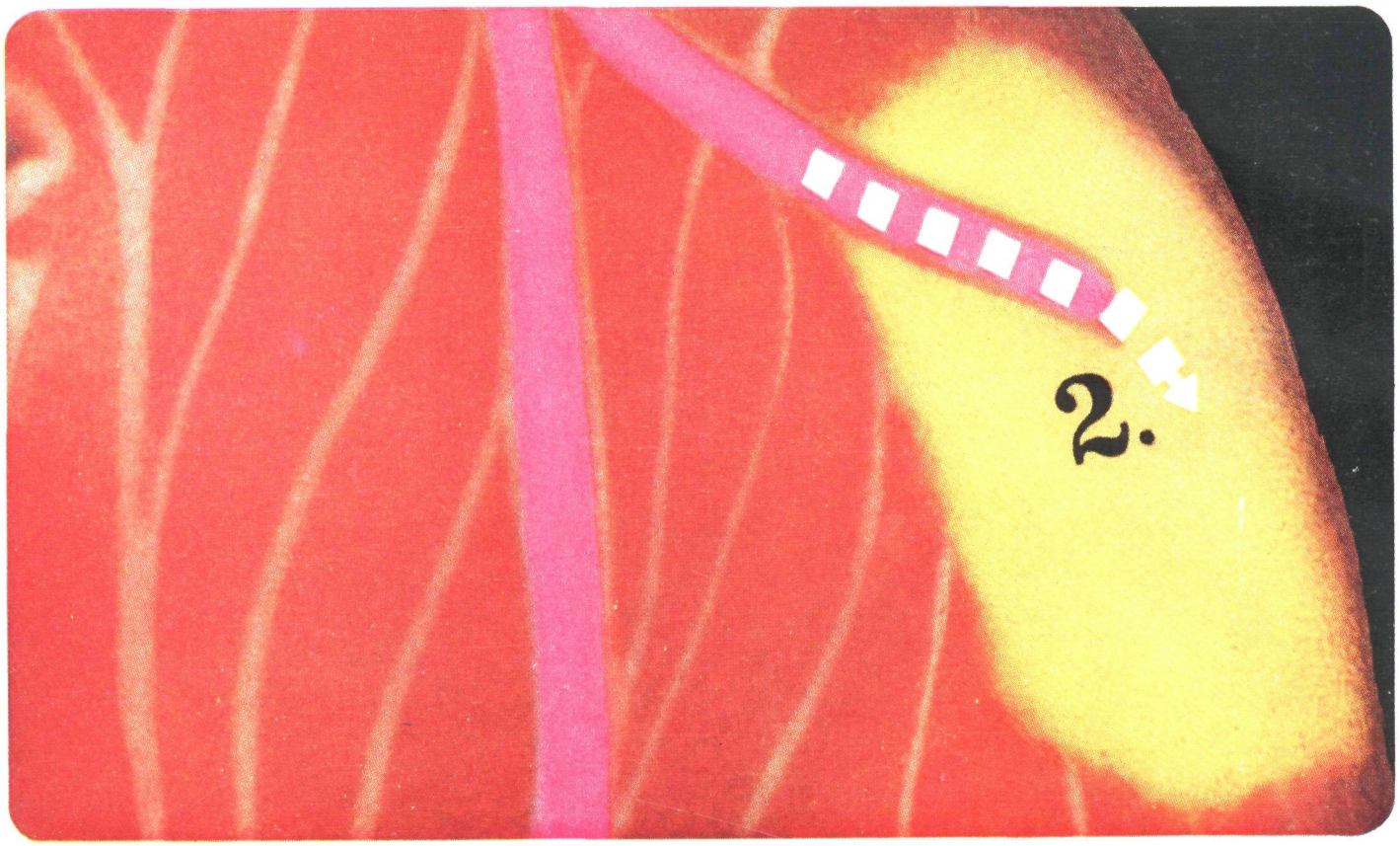
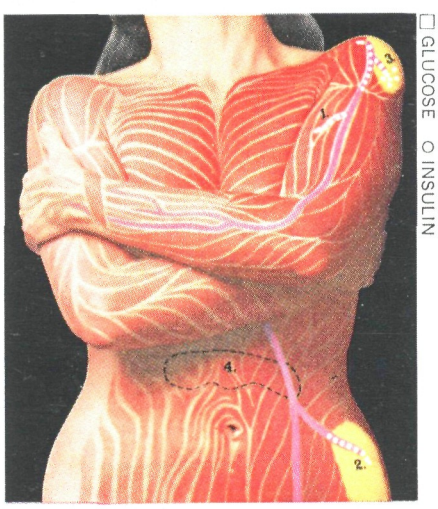
Oral diabetes therapy that does more than just lower blood sugar



2 Only DBI-TD (phenformin HCl) promotes weight loss in the overweight maturity-onset diabetic.

All other oral drugs *except* DBI-TD increase insulin release, which suppresses lipolysis and can accelerate lipogenesis. Thus DBI-TD, by avoiding insulin oversecretion, appears to ease—rather than aggravate—the weight problem in patients unresponsive to diet alone.



...and that's not all

1 Only DBI-TD directs glucose primarily into muscle—where it is most needed.

3 Only DBI-TD helps counterbalance the inefficient action of the diabetic's own insulin.

4 Only DBI-TD, because of its unique action, reduces the risk of hypoglycemic reaction.

a physiological approach to begin with in maturity-onset diabetes

DBI®-TD (phenformin HCl)

timed-disintegration capsules 50 mg.

See adjacent page for brief summary of prescribing information.

Once-daily dosage frees many maturity-onset diabetics from midday-dose worries

Indications: Dymelor is an oral hypoglycemic sulfonylurea indicated in stable, maturity-onset, nonketotic diabetes not controlled solely by diet. Given alone or with phenformin, Dymelor may result in resumption of response to oral therapy in certain patients not controlled initially or secondarily by other oral agents.

Sulfonylurea therapy is no substitute for increased attention to diet and other factors in control of diabetes.

Satisfactory response is usually indicated by reduction of glycosuria and hyperglycemia within seven to ten days. Appearance of glycosuria and ketonuria after withdrawal of Insulin and initiation of Dymelor suggests a need for dosage adjustment or possibly a poor response to Dymelor. In the absence of clinical improvement after dosage adjustment, therapy with Insulin is usually indicated.

Insulin is standard therapy during stress, complications, infections, and surgery. Dymelor can be continued, if tolerated, and Insulin given as supportive treatment.

Contraindications: Juvenile, brittle, unstable, or severe diabetes (on occasion, Dymelor may be given jointly with Insulin); diabetes complicated by acidosis, ketosis, coma, major surgery, infections, gangrene, or severe trauma; pregnancy; renal glycosuria; hyperglycemia associated with uremia; nondiabetic conditions.

Precautions: Inappropriate dosage may result in severe and prolonged hypoglycemia. *Treat immediately with intravenous hypertonic glucose solution (10 to 50 percent), and continue until hypoglycemia subsides.*

Instruct new patients on the management of diabetes, prevention of complications, diet, personal hygiene, methods of testing for glycosuria and ketonuria, and the causes, signs, and prevention of hypoglycemia. A regular follow-up regimen with the physician is imperative.

Use Dymelor with care in patients with hepatic or renal impairment, acute alcoholism, adrenal or pituitary insufficiency, or porphyria; in elderly, debilitated, malnourished, or semistarved patients; and in patients on antimicrobial sulfas, phenylbutazone, or probenecid. Administer thiazide diuretics with caution to patients on sulfonylurea therapy.

Patients receiving sulfonylureas have experienced "disulfiram reactions" following ingestion of alcohol. Sulfonylureas may have an antithyroid effect.

Adverse Reactions: In the changeover from Insulin to Dymelor, hypoglycemia can occur while both drugs are given simultaneously.

Occasional side-effects are G.-I. disturbances, including nausea and gastritis; maculopapular skin eruption or other cutaneous manifestations of hypersensitivity; headache, nervousness, and tingling, all possibly related to hypoglycemia; and elevations in alkaline phosphatase. Rarely, photosensitivity reactions, bleeding from the upper G.-I. tract, jaundice, thrombocytopenia, pancytopenia, agranulocytosis, leukopenia, hemolytic anemia, or aplastic anemia may occur.

Administration and Dosage: Daily dosage may range between 250 mg. and 1.5 Gm. No loading dose should be used. Doses in excess of 1.5 Gm. daily are not recommended.

Patients on 1 Gm. or less daily can be controlled with once-daily dosage. Patients receiving 1.5 Gm. daily usually benefit from twice-daily dosage, before morning and evening meals. Dymelor may be used with phenformin or Insulin.

For full prescribing information, see package literature.

How Supplied: Tablets Dymelor® (acetohexamide, Lilly) (scored), 250 and 500 mg. [111667B]

Additional information available upon request.
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