The Journal of the American Diabetes Association

diabetes

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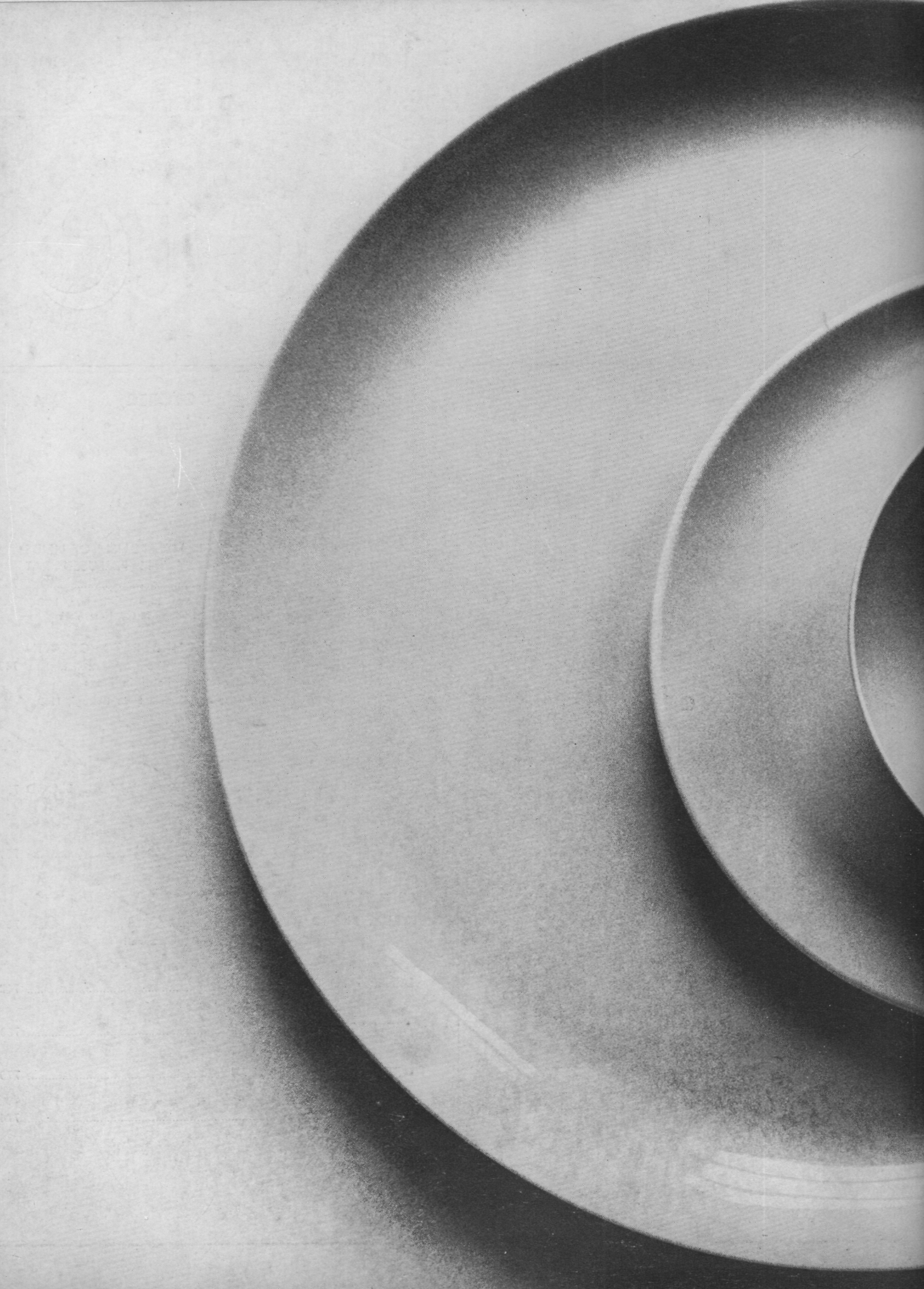

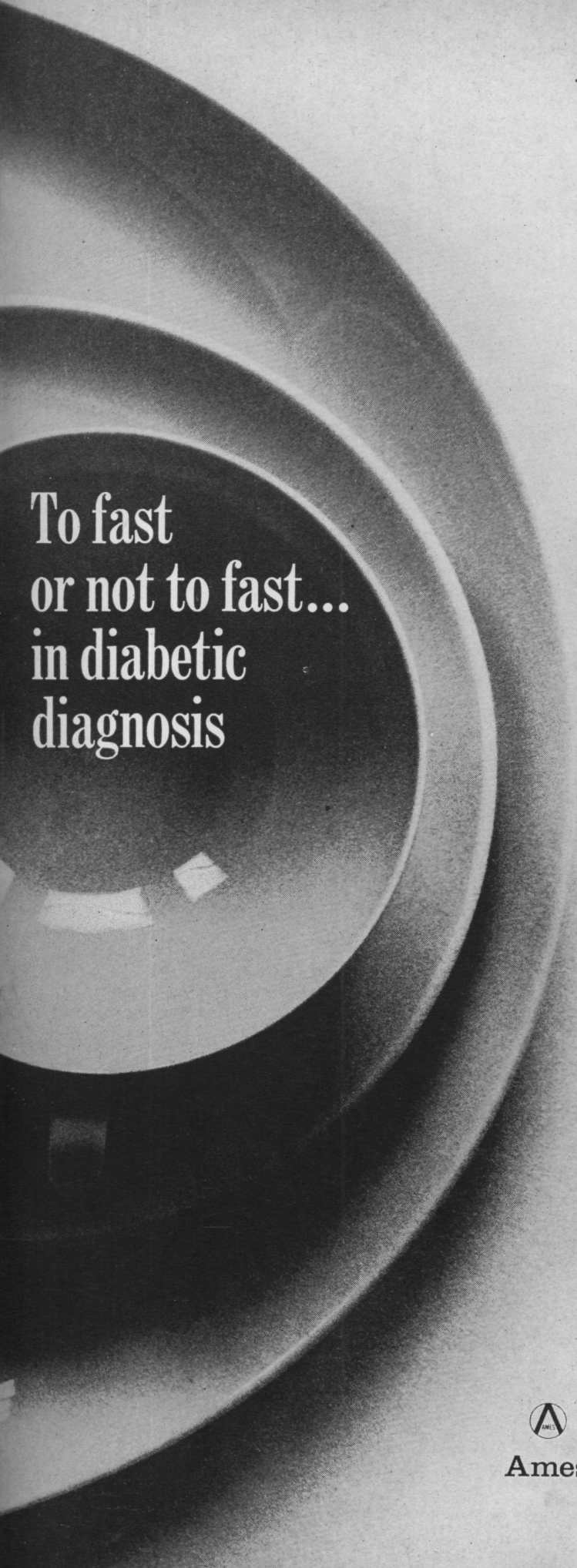

To fast or not to fast... in diabetic diagnosis

Postprandial vs fasting blood glucose

While the fasting blood-sugar level is frequently used as the basis for a diagnosis of diabetes, many adults may escape detection if this is the sole measurement used. Danowski states that "...the most common undiagnosed form of diabetes mellitus in the adult...is characterized by normal fasting blood sugar levels with undue postprandial... hyperglycemia."[1] Lee reports that *"For discovering new cases of diabetes,* postprandial and postglucose determinations are infinitely superior to fasting levels."[2] Adult diabetes, diagnosed in its early stages, is usually amenable to treatment by diet alone or by diet with oral hypoglycemic agents.[1] Such treatment, instituted promptly upon diagnosis, may prevent the diabetic condition from progressing to a more advanced stage with attendant complications.

Reliable diagnostic team

DEXTROSTIX® Reagent Strips—the 60-second test for blood glucose—and GLUCOLA™—pleasant-tasting, well-tolerated carbonated beverage which provides a loading dose equivalent to 75 Gm. of glucose—constitute a dependable product team that provides definitive results in postprandial screening procedures. When you instruct your patient to drink a 7-oz. bottle of GLUCOLA, instead of a regular meal, two hours before scheduling an office test with DEXTROSTIX, you are sure that the glucose challenge is adequate for the reliable screening for diabetes. Unlike the cloying, conventional type glucose loading dose, GLUCOLA is refreshing, avoids nausea and vomiting. In 85,000 patients tested with GLUCOLA not one case of vomiting was reported.[3]

You know the result...before the patient leaves the office

The test with DEXTROSTIX requires only a small globular amount of capillary or venous blood for a reliable quantitative blood-glucose estimate in 60 seconds. With DEXTROSTIX and GLUCOLA, you are able to estimate whether the patient is nondiabetic, diabetic or borderline. It has been suggested that screening levels be set "...low enough, such as 130 mg./100 ml. true glucose one hour or longer after a meal, to pick up all presumed or probable diabetics, who will then be candidates for further testing."[4]

References

(1) Danowski, T. S., *in* Danowski, T. S.; Krosnick, A., and Knowles, H. C., Jr.: *Juvenile Diabetes,* Proceedings of a Workshop Held at Princeton, New Jersey, April 22-23, 1963, p. 3. (2) Lee, C. T., Jr.: M. Clin. North America *44*:1507 (Nov.) 1960. (3) Leonards, J. R.; McCullagh, E. P., and Christopher, T. C.: Diabetes *14*:96 (Feb.) 1965. (4) Krall, L. P.: M. Clin. North America *49*:893 (July) 1965.

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Product team

a palatable glucose challenge
for reliable postprandial readings

for easy-to-perform blood-glucose screening
while the patient is still in your office

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Effectiveness—The hypoglycemic activity of Dymelor following a morning dose generally extends throughout the twenty-four-hour period.[1]

Safety—The gradual reduction of effect usually prevents undue depression of blood sugar during the sleeping hours. Cumulation of the drug ordinarily does not occur.[2]

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1. Wood, F. C., and Williams, R. H.: Oral Drug Therapy of Diabetes Mellitus, GP, *33*:128 (April), 1966.

2. Galloway, J. A., *et al.*: The Metabolism of Acetohexamide in Man, Diabetes, *14*:456, 1965.

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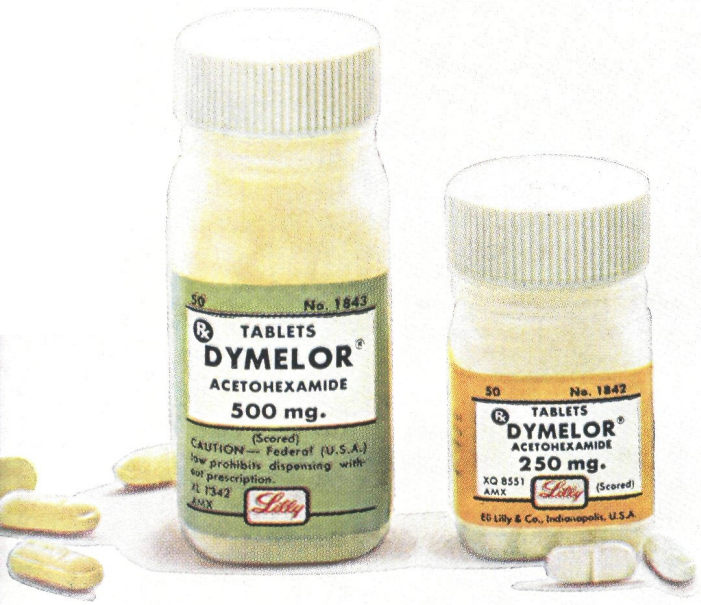

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Indications: Dymelor is indicated only in the treatment of diabetes mellitus of the stable, maturity-onset, nonketotic type in patients not controlled solely by dietary regulation. A trial with Dymelor, either alone or in combination with phenformin, may result in a resumption of response to oral therapy in certain patients who have failed to be controlled either initially or secondarily with the other oral agents.

Contraindications: The use of Dymelor is contraindicated as follows:

1. As sole treatment in juvenile, brittle, unstable, or severe diabetes, because sulfonylurea drugs as a class are ineffective when employed as the only therapy in these types of diabetes. Insulin is the required therapeutic agent in such cases, although, on occasion, Dymelor may be given jointly with Insulin.
2. In diabetes complicated by acidosis, ketosis, coma, major surgery, infections, gangrene, or severe trauma.
3. In pregnancy.
4. In patients with renal glycosuria or the hyperglycemia occasionally associated with uremia. (The hyperresponsiveness of such patients to sulfonylurea drugs may result in prolonged or fatal hypoglycemia.)
5. In patients who do not have diabetes.

Precautions: Dymelor is a potent hypoglycemic agent, and excessive dosage may result in severe hypoglycemia which requires prompt and vigorous treatment (see below). For this reason, the dosage recommendations for Dymelor should be followed carefully.

The new diabetic starting on Dymelor must receive full instructions in the basic principles of diabetic management, including prevention of complications, dietary regulation, methods of testing the urine for glucose and ketone bodies, and the cause, signs, and prevention of hypoglycemia.

If hypoglycemia is prolonged or recurs, treatment with intravenous hypertonic glucose solution (10 to 50 percent) should be instituted immediately and continued until the hypoglycemic tendency subsides.

A regular follow-up regimen with the physician is imperative.

Patients with hepatic and/or renal impairment, as well as those who are debilitated or malnourished, must be observed very closely for hypoglycemia. In these patients, careful dosage adjustments and close observation are in order.

Because of the sulfonylurea-potentiating effects reported with certain drugs, hypoglycemia may occur when such agents as the antimicrobial sulfas, phenylbutazone, or probenecid are a part of the treatment program of patients receiving Dymelor.

Dymelor should be used cautiously in elderly persons and in patients with acute alcoholism or adrenal or pituitary insufficiency.

Short-term studies of patients treated with Dymelor have demonstrated no significant changes in thyroid function, although this class of drugs may have an antithyroid effect.

Diabetes and porphyria rarely occur together. In the event they do, sulfonylurea compounds, like the antimicrobial sulfa drugs and barbiturates, may aggravate hepatic porphyria.

Very rarely, patients receiving any of the sulfonylureas may experience peculiar symptoms, referred to as the "disulfiram reaction," following the ingestion of alcohol.

In view of cases of liver damage reported with all sulfonylurea agents, Dymelor should be used with great caution in the presence of liver disease; such patients should be observed closely, and follow-up clinical and laboratory examinations should be performed, particularly with respect to liver function studies.

Thrombocytopenia and pancytopenia in association with the use of Dymelor have been reported in rare instances. Because agranulocytosis, leukopenia, hemolytic anemia, aplastic anemia, and cholestatic jaundice have resulted occasionally with other sulfonylurea drugs, the possibility of the occurrence of these untoward reactions should be kept in mind when Dymelor is prescribed.

Caution should be exercised in the administration of thiazide diuretics to diabetic patients on sulfonylurea therapy since the thiazides have been reported to aggravate the diabetic state and to result in increased requirements of the sulfonylurea, temporary loss of control, or even secondary failure.

Side-Effects: Although hypoglycemia is a manifestation of the activity of the drug and is not a side-effect in the usual sense, it is nevertheless desirable to avoid this reaction.

Patients receiving sulfonylurea drugs may also experience gastro-intestinal disturbances, including nausea, gastritis, and, rarely, bleeding from the upper gastro-intestinal tract. Cutaneous manifestations of hypersensitivity, characterized by the development of maculopapular skin eruption or other dermatoses, have been reported, and a few instances of headache, nervousness, and tingling, all possibly related to hypoglycemia, have also been noted. Photosensitivity reactions may occur.

Jaundice of the mixed hepatocellular type has been observed with Dymelor but is very unusual. Elevations in alkaline phosphatase have been reported in some patients receiving Dymelor as well as in some cases treated with other sulfonylureas. The significance of these changes is unknown, since diabetics as a group may have higher values for certain liver function tests than do nondiabetics.

How Supplied: Dymelor is supplied as scored tablets of 250 mg. and 500 mg. in bottles of 50, 200, and 500.

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THIS UNIQUE MAGAZINE Helps Patients Understand Diabetes!

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here was a time when it was thought that all diabetics were insulin deficient...

BUT THAT WAS BEFORE new techniques demonstrated that overweight, stable adult diabetics may have excessive postprandial levels of circulating insulin.

NEW RESEARCH is focusing attention on metabolic problems of the overweight, stable adult (ketoacidosis-resistant) diabetic and suggests that DBI-TD is the product of choice together with a proper diet in the management of these patients. For the ketoacidosis-prone diabetic, insulin is still the essential hypoglycemic agent.

THE PROBLEMS	A PRACTICAL SOLUTION
Insulin release in response to hyperglycemia is excessive	DBI-TD lowers blood sugar and may reduce excessive insulin release toward normal
Fat mobilization and utilization are suppressed and lipogenesis accelerated by excessive endogenous insulin	DBI-TD lowers blood sugar without promoting lipogenesis; permits fat mobilization and utilization
Hyperglycemia, glycosuria and ketoacidosis resistance with continued weight gain or maintained obesity	DBI-TD lowers blood sugar, controls glycosuria and aids in gradual weight loss*

*Anorexia has been suggested as a possible basis for weight loss. However, controlled studies suggest that it is due to the mechanism of drug action. Comparable dosages of DBI-TD do not induce weight loss or lower blood sugar in nondiabetic subjects.

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Dosage: 1 to 3 capsules daily. **Side Effects:** Gastrointestinal, occurring more often at higher dosage levels, abate promptly upon dosage reduction or temporary withdrawal. **Precautions:** Occasionally an insulin-dependent patient will show "starvation" ketosis (acetonuria without hyperglycemia) which must be differentiated from "insulin-lack" ketosis which is accompanied by acidosis, and treated accordingly. Lactic acidosis has been reported in nondiabetics and diabetics treated with insulin, with diet, and with DBI. Question has arisen regarding possible contribution of DBI to lactic acidosis in patients with renal impairment and azotemia and also those with severe hypotension secondary to myocardial or bowel infarction. Periodic B. U. N. determinations should be made when DBI is administered in the presence of chronic renal disease. DBI should not be used when there is significant azotemia. Any cardiovascular lesion that could result in severe or sustained hypotension, which may itself lead to development of lactic acidosis, should be considered cause for immediate discontinuation of DBI at least until normal blood pressure has been restored and is maintained without vasopressors. Should lactic acidosis occur from any cause, vigorous attempts should be made to correct circulatory collapse, tissue hypoxia, and pH. **Contraindications:** Severe hepatic disease, renal disease with uremia, cardiovascular collapse. Not recommended without insulin in acute complications of diabetes (metabolic acidosis, coma, severe infections, gangrene, surgery). **Pregnancy Warning:** *During pregnancy, until safety is proved, use of DBI, like other oral hypoglycemic drugs, is to be avoided.*

Consult product brochure.

Also available: DBI tablets 25 mg.

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For your newly diagnosed, adult diabetic **Orinase®** the standard of comparison for effectiveness and safety

the of Orinase (tolbutamide)

Contraindications: Do not use as sole therapy in juvenile diabetes, unstable or brittle diabetes or diabetes complicated by acidosis, ketosis, coma. Fever, severe trauma, major surgery, severe diarrhea, nausea or vomiting may require supplemental insulin. Do not use in patients with severe renal insufficiency or persistent skin reactions. Tolbutamide has feticidal and teratogenic effects in animals at doses of 1000 to 2500 mg./kg. per day. Safety and usefulness during pregnancy not yet established; not recommended in obstetrical patients. **Precautions:** Observe all measures indicated with insulin. Instruct patient fully concerning his disease and consequences of dietary neglect, weight control, exercise, hygiene, avoidance of infection and need for informing physician of any unusual feeling. Teach patient to recognize and counteract impending hypoglycemia and test for glycosuria and ketonuria. During insulin withdrawal, take care to avoid ketosis, acidosis and coma. Thiazide diuretics may aggravate diabetes; administer with caution to patients on tolbutamide. Careful observation and dosage adjustment essential in patients with impaired hepatic and/or renal function and debilitated, malnourished or semistarved patients because of increased danger of severe hypoglycemia, which may require several days to correct. **Side Effects:** Severe hypoglycemia, which may mimic acute neurologic disorders, is uncommon, but hepatic and/or renal disease, malnutrition, debility, advanced age, alcoholism, adrenal and pituitary

flexibility

With Orinase, the physician can readily and safely adjust dosage—from patient to patient, or from time to time in a particular patient—to meet variations in metabolism or changing circumstances. Dosage flexibility, a major factor in successful oral control, may make all the difference in maintaining satisfactory, smooth response to treatment.

insufficiency may predispose to it. The following may prolong or enhance the action of tolbutamide and increase the risk of hypoglycemia: insulin, phenformin, sulfonamides, oxyphenbutazone, phenylbutazone, salicylates, probenecid and monoamine oxidase inhibitors. Reduction of RAI uptake after long use, without evidence of hypothyroidism or thyroid enlargement, has been reported. Photosensitivity reactions and disulfiram-like reactions have occurred after ingestion of alcohol. Crystalluria or other renal effects have not been observed. Jaundice rare; has cleared after drug withdrawal. In persistent jaundice, rule out carcinoma of pancreas or other obstructive lesions of the bile duct. Leukopenia, agranulocytosis, thrombocytopenia and hemolytic anemia have been reported. Other reactions usually mild—headache, nausea, epigastric fullness, heartburn—frequently disappear when dosage reduced or given in divided doses with meals. Allergic skin reactions (pruritus, erythema, and urticarial, morbilliform, or maculopapular eruptions) frequently disappear with continued administration. **Supplied:** 0.5 Gm. scored tolbutamide tablets in bottles of 50, 200 and 500. **For more detailed prescribing information on this product, consult your Upjohn representative or see the package circular.**

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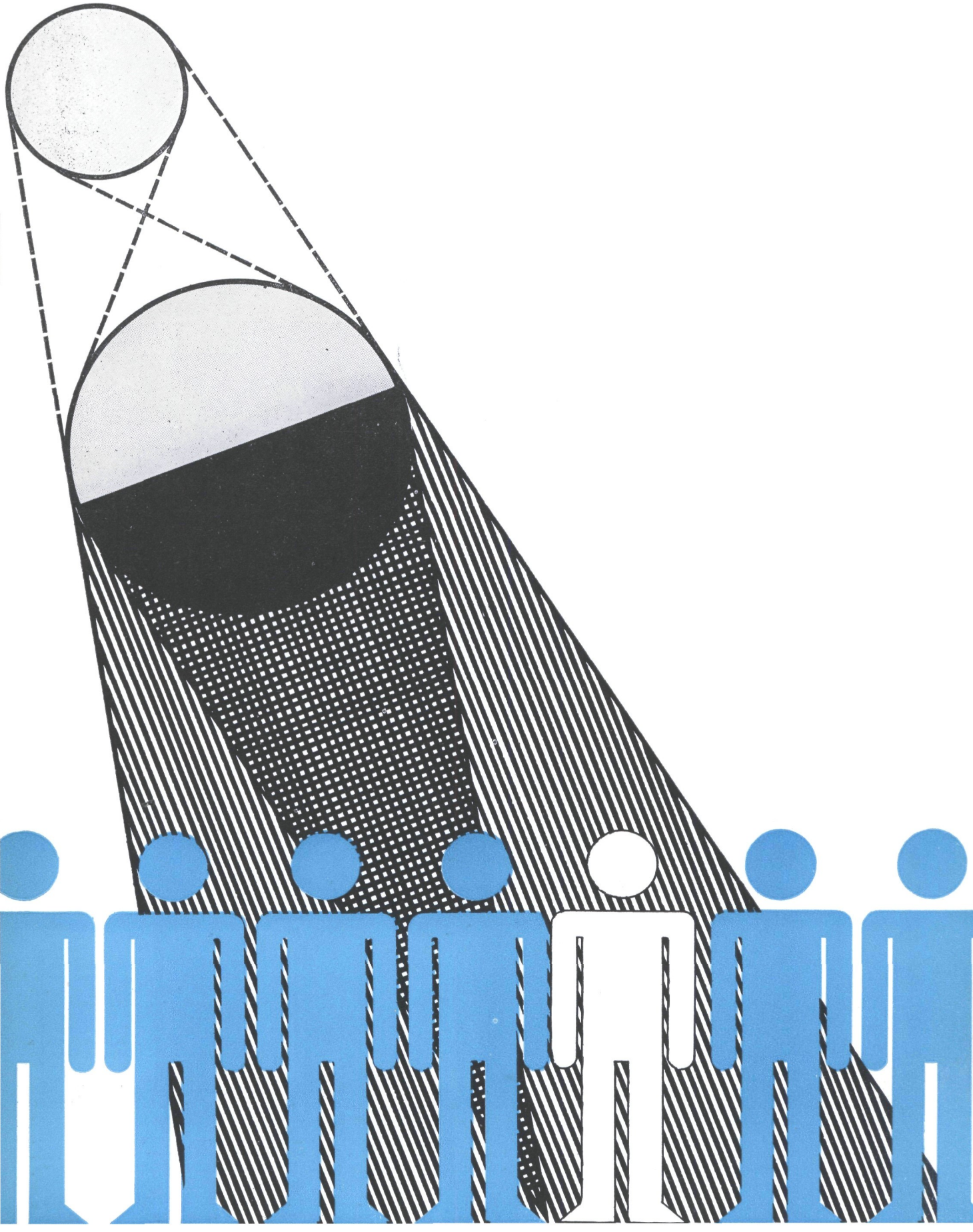


for the diabetic patient in penumbra*

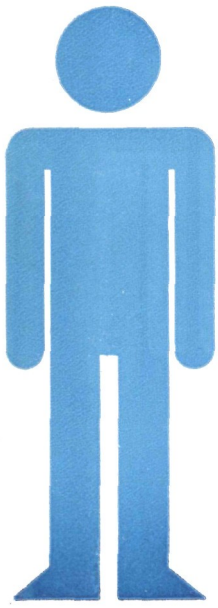
In stable, maturity-onset diabetes, some patients are not at all amenable to oral therapy; many are well controlled and encounter no difficulties. Between these extremes, there is the diabetic patient in penumbra--the secondary failure, the patient with untoward side reactions, or the insufficiently responsive patient. For these diabetics in penumbra, Upjohn research has developed a new therapeutic recourse--Tolinase, an effective sulfonylurea. In most patients, once-a-day therapy is satisfactory. Tolinase may control diabetes where other oral agents fail ... it may be well tolerated where other oral agents are not.

*Penumbra: a marginal region or borderland of partial obscurity or of some blighting influence. (Webster's Unabridged International Dictionary, Second Edition, 1957.)

new

Tolinase® (tolazamide)

extends the domain of oral control in diabetes



Contraindications: *Do not use in juvenile diabetes, unstable or* brittle diabetes or in diabetics undergoing surgery or those with infections, severe trauma, ketosis, acidosis or coma, or a history of repeated ketoacidosis. Do not use in patients with renal, hepatic or endocrine disease. Safety and usefulness during pregnancy not established; not recommended in obstetrical patients. **Precautions:** Observe all measures indicated with insulin or other sulfonylureas. Instruct patient fully concerning his disease and consequences of dietary neglect, careless attitude, the importance of weight control, exercise, hygiene, avoidance of infection and need for informing physician of any unusual feeling. Teach patient to recognize and counteract impending hypoglycemia and test for glycosuria and ketonuria. During insulin withdrawal, take care to avoid ketosis, acidosis and coma. Patients previously treated with phenformin plus sulfonylureas, being transferred to therapy with tolazamide, should be carefully observed during the transitional period. Thiazide diuretics may aggravate diabetes; administer with caution to patients on tolazamide. *Careful observation and dosage adjustment is essential in debilitated, malnourished or semi-starved patients because of the increased danger of severe hypoglycemia, which may require corrective therapy. Advanced age, alcoholism, hepatic and* renal disease, adrenal and pituitary insufficiency may also predispose to severe hypoglycemia which may mimic acute neurologic disorders. The following may enhance the action of tolazamide and increase the risk of hypoglycemia: insulin, phenformin, sulfonamides, oxyphenbutazone, phenylbutazone, salicylates, probenecid and monoamine oxidase inhibitors. **Side Effects:** Hypoglycemia observed in 2.2% of 1,784 cases; may usually be alleviated by reducing the dose (see Precautions for factors possibly increasing danger of hypoglycemia). Gastrointestinal symptoms related to Tolinase therapy were nausea 0.6%, vomiting 0.3%, and gas 0.2%. Dermal reactions consisted of rash 0.3%, and pruritus 0.1%. Weakness, fatigue, dizziness, vertigo, malaise and headache, each less than 0.1%, may not have been drug related. Leukopenia occurred in a few patients, but the count returned to normal with continued administration of drug. Although disulfiram-like alcoholic flushes have not been reported with Tolinase, their possibility should be kept in mind. **Supplied:** 100 mg. and 250 mg. compressed, scored tablets in bottles of 50. **For more detailed prescribing information on this product, consult your Upjohn representative or see the package circular.**

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HE WILL ALWAYS NEED YOU

...but you can make his diabetes easier to manage with Diabinese

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Your patient treated with Diabinese is less likely to experience early drug failure: Better regulation with Diabinese increases the likelihood of *continuing* response.

	Treated with tolbutamide	Treated with Diabinese
After one month:	(432 patients)	(305 patients)[2]
Patients with EXCELLENT CONTROL*	38%	52%
Rate of Secondary Failure†	27%	12%

*Below 130 mg./100 ml.; no glycosuria, no diabetic symptoms.
†After six years of therapy, 34% of the tolbutamide patients had failed as compared with only 15% of patients receiving Diabinese.

Greater effectiveness with lower dosage provides the reserve potency that may be required to forestall drug failure: "Early use of a more potent drug, before the patient is out of control, is preferable since it means greater reserve, and thus avoids the need for a later change."[3]

Pfizer

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chlorpropamide

makes diabetes easier to manage...easier to live with

turn page for brief summary and references...

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chlorpropamide

makes diabetes easier to manage
easier to live with

Contraindications: Diabinese is not indicated as the sole agent in juvenile diabetes, severe or unstable brittle diabetes, and diabetes complicated by acidosis, coma, surgery, infections, severe trauma, severe diarrhea, or nausea and vomiting. Contraindicated in patients with impairment of hepatic, renal or thyroid function, and during pregnancy. Serious consideration should attend its use in women of child-bearing age. Use with caution in patients with Addison's disease and those receiving barbiturates or ingesting alcohol.

Warnings: Prescription refills should be controlled by the physician. Urine tests for sugar and acetone three times daily and complete weekly medical evaluations are necessary during the first six weeks of therapy. Frequent liver function tests may be indicated. *Increase in serum alkaline phosphatase may indicate incipient jaundice and the drug should be withdrawn.*
Chlorpropamide-Phenformin: In infection, severe trauma or surgical procedures, temporary withdrawal of chlorpropamide-phenformin therapy and substitution of insulin, alone or with chlorpropamide, may be necessary.

Precautions: Hypoglycemic reactions may occur. They are treated by glucose administration. Treat under close observation for at least 3 to 5 days.
Insulin is essential during intercurrent complications.
Chlorpropamide-Phenformin: Gastrointestinal upset indicates reduction of phenformin dosage. Lactic acidosis and ketonuria without hypoglycemia have been reported with phenformin.

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; infrequently weakness and paresthesias, leukopenia, thrombocytopenia and mild anemia; rarely aplastic anemia, agranulocytosis and phototoxicity. Not related to dosage is idiosyncrasy or hypersensitivity, rarely severe. Any hypersensitivity reaction dictates discontinuance of therapy. This includes skin rash (rarely erythema multiforme or exfoliative dermatitis), low grade fever, eosinophilia, progressive elevation of alkaline phosphatase, possibly depression of formed elements of the blood and rarely severe diarrhea with bleeding associated with jaundice, skin rash or both.

Supply: 100 mg. and 250 mg. scored tablets.

More detailed professional information available on request.

References: 1. Dunlop, D.: St. Bartholomew's Hosp. J. 67:159, July, 1963. 2. Moss, J. M. et al.: Scientific Exhibit, Fifth Cong. Int. Diabetes Fed., Toronto, Canada, July 20-24, 1964. 3. Beaser, S. B.: Scientific Exhibit, A. M. A. Ann. Meet., San Francisco, Calif., June 21-25, 1964.

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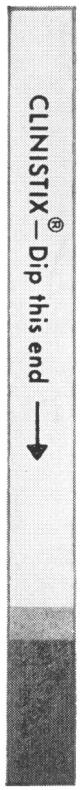

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