



# diabetes

## CONTENTS

**JULY** **1968**  
Volume 17 • Number 7

### ORIGINAL CONTRIBUTIONS

**GLUCOSE UPTAKE AND PRODUCTION DURING THE ORAL GLUCOSE TOLERANCE TEST** ..... 415

Robert Steele, Ph.D., Clara Bjerknes, B.A., Isbel Rathgeb, Ph.D., and Norman Altszuler, Ph.D., Upton, New York, and New York

**GLUCOSE-FATTY ACID INTERACTIONS IN THE RAT DIAPHRAGM IN VIVO** ..... 422

Gustav Schonfeld, M.D., and David M. Kipnis, M.D., St. Louis

**INSULIN DISPOSITION IN THE ISOLATED PERFUSED RAT HEART** ..... 427

Effect of "Bound" Insulin

Barry I. Posner, M.D., Stuart L. Sotman, B.S., and Harry N. Antoniades, Ph.D., Boston

**EFFECTS OF ACUTE EXPERIMENTAL PANCREATITIS ON INSULIN METABOLISM IN THE DOG** ..... 437

Application of a New Equilibrium Infusion Technic

Xavier Pi-Sunyer, M.D., John J. Byrne, M.D., and Norbert Freinkel, M.D., Boston

**STUDIES OF A SIMPLIFIED PLASMA INSULIN IMMUNO-ASSAY USING CELLULOSE POWDER** ..... 444

Daniel S. Zaharko, Ph.D., and Lyle V. Beck, Ph.D., Bloomington, Indiana

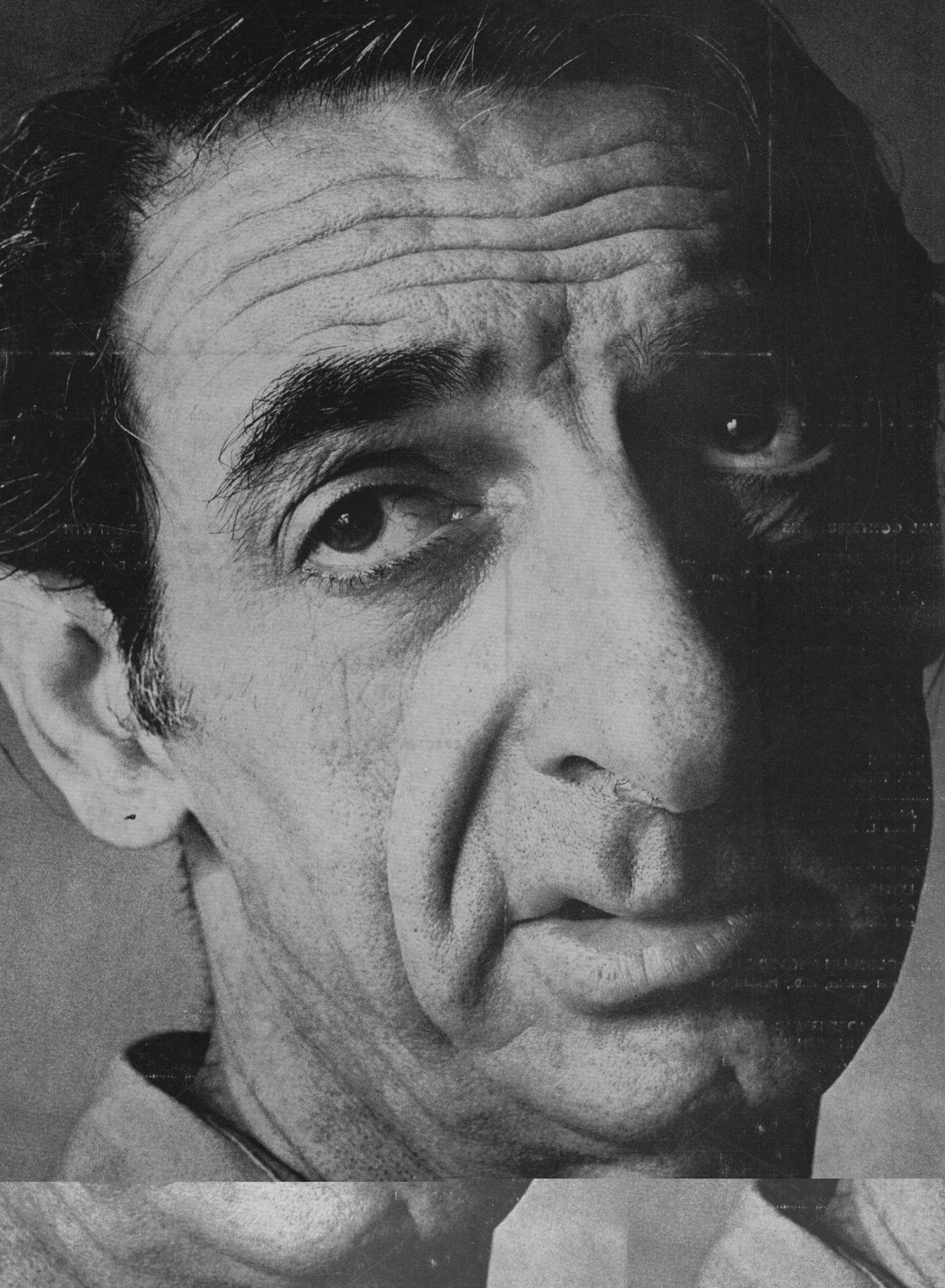
**A THREE-YEAR TRIAL OF ATROMID THERAPY IN EXUDATIVE DIABETIC RETINOPATHY** ..... 458

L. J. P. Duncan, M.B., B.Sc., F.R.C.P. (Ed.), J. F. Cullen, M.Ch., F.R.C.S., J. T. Ireland, M.B., M.R.C.P. (Ed.), J. Nolan, M.B., F.R.C.S. (Ed.), B. F. Clarke, M.B., M.R.C.P. (Ed.), and M. F. Oliver, M.D., F.R.C.P. (Ed.), Edinburgh

**ABSTRACTS** ..... 468

**ORGANIZATION SECTION** ..... 472

**NEWS NOTES** ..... 473



# The Dropout

At first his diabetes was well controlled with an oral agent. Then the drug stopped working. His blood sugar went up and up. He became a dropout from oral therapy—a secondary failure—until he was rescued by Diabinese.

Diabinese often rescues the dropouts from other oral hypoglycemic therapy. It restores control, gives the convenience of once-a-day dosage, saves money.

If he'd been on Diabinese from the

very beginning, he could have saved money from the very beginning. He could have had the simplicity of once-a-day dosage from the very beginning. And he might never have become a dropout. True secondary drug failures are few and far between with Diabinese.

Your Pfizer Representative has facts and figures at his fingertips about the economy and the long-term advantages of Diabinese therapy. He'll gladly share his information with you.

It makes good sense to start with

**Diabinese®**  
**(chlorpropamide)**



LABORATORIES DIVISION

turn page for brief summary...

# Diabinese® (chlorpropamide)

**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.

**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.*



**LABORATORIES DIVISION**

New York, N. Y. 10017

## TWO NEW 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. 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.

# DIABETES®

## The Journal of the American Diabetes Association

EDITOR, HARVEY C. KNOWLES, JR., M.D., *Cincinnati*

ASSOCIATE EDITORS: DAVID M. KIPNIS, M.D., *St. Louis* • HENRY T. RICKETTS, M.D., *Chicago*

ADVISORY EDITORS: CHARLES H. BEST, M.D., *Toronto* • FRANK N. ALLAN, M.D., *Boston*

ABSTRACTS EDITOR, JOHN A. GALLOWAY, M.D., *Indianapolis* • MANAGING EDITOR, EDWARD W. SANDERSON, *New York*

ART EDITOR, W. I. VAN DER POEL, *New York*

### EDITORIAL BOARD

TERM EXPIRING DECEMBER 1968

JAMES ASHMORE, PH.D., *Indianapolis*  
RUBIN BRESSLER, M.D., *Durham*  
FREDERICK C. GOETZ, M.D., *Minneapolis*  
CHRISTIAN R. KLIMT, M.D., DR. P.H.,  
*Baltimore*  
ARNOLD LAZAROW, M.D., PH.D., *Minneapolis*  
RACHMIEL LEVINE, M.D., *New York*  
ALEXANDER MARBLE, M.D., *Boston*  
THEODORE B. VAN ITALLIE, M.D., *New York*

TERM EXPIRING DECEMBER 1969

GEORGE F. CAHILL, JR., M.D., *Boston*  
MARVIN CORNBLATH, M.D., *Chicago*  
THADDEUS S. DANOWSKI, M.D., *Pittsburgh*  
C. F. GASTINEAU, M.D., *Rochester, Minn.*  
PAUL E. LACY, M.D., *St. Louis*  
VAUN A. NEWILL, M.D., *Cincinnati*  
MARVIN D. SIPERSTEIN, M.D., PH.D.,  
*Dallas*  
GERALD A. WRENSHALL, PH.D., *Toronto*

TERM EXPIRING DECEMBER 1970

JOHN W. ENSINCK, M.D., *Seattle*  
STEFAN S. FAJANS, M.D., *Ann Arbor*  
PETER H. FORSHAM, M.D., *San Francisco*  
GEROLD M. GRODSKY, PH.D., *San Francisco*  
PHILIP M. Lecompte, M.D., *Boston*  
IRVING H. LEOPOLD, M.D., *New York*  
ROGER H. UNGER, M.D., *Dallas*  
PETER H. WRIGHT, M.D., *Indianapolis*

TERM EXPIRING DECEMBER 1968

BURIS R. BOSHELL, M.D., *Birmingham, Ala.*  
WAYNE V. GREENBERG, M.D., *Augusta, Ga.*  
RONALD K. KALKHOFF, M.D., *Milwaukee*  
CHARLES A. ROSENBERG, M.D., *Washington, D.C.*  
THOMAS G. SKILLMAN, M.D., *Omaha*  
LEON S. SMELO, M.D., *Birmingham, Ala.*

TERM EXPIRING DECEMBER 1969

MARIOS C. BALODIMOS, M.D., *Boston*  
SAMUEL B. BEASER, M.D., *Boston*  
ARTHUR R. COLWELL, JR., M.D., *Wilmette, Ill.*  
HIROMICHI T. NARAHARA, M.D., *St. Louis*  
OTAKAR V. SIREK, M.D., PH.D., *Toronto*  
ELEANOR A. WASKOW, M.D., *Phoenix*

TERM EXPIRING DECEMBER 1970

JOSEPH D. BROWN, M.D., *Iowa City*  
RICHARD A. CHERRY, M.D., *Hayward, Calif.*  
PAUL S. ENTMACHER, M.D., *New York*  
BERT F. KELTZ, M.D., *Oklahoma City*  
CHARLES R. SHUMAN, M.D., *Philadelphia*

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.

Matter appearing in DIABETES is copyrighted. Permission to reproduce all or part of papers appearing in it may be granted on application, under appropriate conditions and if proper credit is given. Such permission should be requested by written application to the Secretary of the Association.

All signed articles and editorials are the responsibility of the author(s) and not that of the American Diabetes Association.

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 lectures) 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.

Galley proofs are sent to the principal author of each paper, with a price list and order blank for reprints.

All manuscripts and editorial correspondence should be addressed to the Editorial Office, DIABETES, American Diabetes Association, Inc., 18 East 48th Street, New York, New York 10017.

### Subscription and Advertising Information

American Union, \$14.00 per year; elsewhere, \$16.00 per year. Individual copies available at \$1.50 each.

Medical students and physicians within five years after completion of medical school and bioscientists who are predoctoral or not more than two years postdoctoral: \$7.00 per year.

Correspondence concerning subscriptions should be addressed to the Subscription Department, DIABETES. Checks, money orders and drafts for

subscriptions should be made payable to the American Diabetes Association, Inc., and sent to the aforementioned address.

All inquiries about advertising and other business matters should be addressed to the Executive Director of the American Diabetes Association. The publishers reserve in their full discretion the right to accept or reject any proposed advertising and the right to cancel any advertising contract.

DIABETES: The Journal of the American Diabetes Association is published every month by the Association at 18 East 48th Street, New York, New York 10017. Entire contents copyright 1968 by the American Diabetes Association, Inc.; all rights reserved. SECOND CLASS POSTAGE PAID AT NEW YORK, N.Y.

Members receive the Journal as part of their membership privileges. The annual subscription rates for nonmembers are as follows: United States, U. S. Possessions, Canada and the Pan-

# Tomorrow's self-made man needs a break today.

And local businessmen can give it to him. Now. This summer. While there's still time.

Thousands of deserving youngsters are waiting for jobs. Waiting for a chance to work at becoming better citizens.

The corporate giants are already hiring. The Government is already helping.

But we need to reach Main Street. We need to reach you. Because without the support of every local businessman, we cannot succeed. What can you do?

## **Each one hire one.**

Hire one young man or woman. Hire more if you can. But, at least hire one.

No business is too small to help. Think about an extra pair of hands for the summer. Think about a bright youngster filling in vacation gaps. Think about next summer—and the one after that—when you'll have an "experienced beginner" to call on for extra help.

Do yourself a favor. Give a kid a break this summer. Do it now. Call the National Alliance of Businessmen office in your city.

SUMMER  
**JOBS**  
NOW

National Alliance of Businessmen



advertising contributed for the public good.



**He is diabetic,  
he is middle-aged,  
when he needs an antibiotic  
he may be a candidate for**

## **DECLOSTATIN® 300**

Demethylchlortetracycline HCl 300 mg  
and Nystatin 500,000 units  
CAPSULE-SHAPED TABLETS Lederle

**b.i.d.**

To guard susceptible patients against intestinal monilial overgrowth during broad-spectrum therapy—the protection of nystatin is combined with demethylchlortetracycline in DECLOSTATIN.

For your susceptible candidates, prescribe DECLOSTATIN—the broad-spectrum therapy that prevents monilial overgrowth.

**Contraindication:** History of hypersensitivity to demethylchlortetracycline or nystatin.

**Warning:** In renal impairment, usual doses may lead to excessive accumulation and liver toxicity. Under such conditions, lower than usual doses are indicated, and, if therapy is prolonged, serum level determinations may be advisable. A photodynamic reaction to natural or artificial sunlight has been observed. Small amounts of drug and short exposure may produce an exaggerated sunburn reaction which may range from erythema to severe skin manifestations. In a smaller proportion, photoallergic reactions have been reported. Patients should avoid direct exposure to sunlight and discontinue drug at the first evidence of skin discomfort. Necessary subsequent courses of treatment with tetracyclines should be carefully observed.

**Precautions:** Overgrowth of nonsusceptible organisms may occur. Con-

stant observation is essential. If new infections appear, appropriate measures should be taken.

In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

**Side Effects:** Gastrointestinal system—*anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani.* Skin—*maculopapular and erythematous rashes; a rare case of exfoliative dermatitis has been reported.* Photosensitivity; *onycholysis and discoloration of the nails (rare).* Kidney—*rise in BUN, apparently dose related.* Transient increase in urinary output, sometimes accompanied by thirst (rare). Hypersensitivity reactions—*urticaria, angioneurotic edema, anaphylaxis.* Teeth—*dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood.* Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs, discontinue medication and institute appropriate therapy.

**Average Adult Daily Dosage:** 150 mg q.i.d. or 300 mg b.i.d. Should be given 1 hour before or 2 hours after meals, since absorption is impaired by the concomitant administration of high calcium content drugs, foods and some dairy products. Treatment of streptococcal infections should continue for 10 days, even though symptoms have subsided.

LEDERLE LABORATORIES, A Division of American Cyanamid Company,  
Pearl River, New York



# What if today you switched every one of your diabetics on oral agents to Dymelor® Acetohexamide



## ...what could you expect?

At the very least, most of your patients would do just as well. Many of them might do better. (In one group of 689 patients who were taking other oral agents, 46 percent did better when switched to Dymelor; 45 percent did as well. Only 9 percent had been under better control with their previous agent.\*) But beyond good control, there are several other reasons to consider Dymelor.

**Once-daily dosage**, effective for most patients on Dymelor, reduces the risk of patients' missing doses or taking tablets at wrong intervals.

**Flexibility** is provided by the wide dose range. Sel-

dom will you have to transfer patients to another drug. You can adjust dosage within the 250 to 1,500-mg. range as conditions vary or daily habits change.

**Economy** in prescription costs will be appreciated by many patients switched to Dymelor. Because of its relative potency, Dymelor may control many patients at about half the dosage of the short-acting sulfonylurea.

*Patient Starter Kits, useful in establishing therapy with Dymelor, are available from your Lilly representative.*

\*Data compiled from reports of clinical investigators, on file at the Lilly Research Laboratories.

**Indications:** Dymelor® (acetohexamide, Lilly) 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 alcohol-

ism, 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., in bottles of 50, 200, and 500. [111667A]

Additional information available to physicians upon request. Eli Lilly and Company, Indianapolis, Indiana 46206.

