">" is shown in the first column, with a comment in the last column. The computer alarm setting in case of actual blood glucose concentrations exceeding the preselected upper or lower limits is an important feature not supplied by the Biostator. Deviations from the target blood glucose concentrations may occur gradually over time and, therefore, may be missed by the Biostator without instantaneous alarm. Errors signaled by the Biostator result in an alarm and a question mark in the first column. The *hold* mode of the Biostator is marked by an *H* and a comment. The program can be stopped by pressing Q (*quit*) on the keyboard. This results in an immediate interruption of data acquisition, the screen is cleared, and the names of written data files are shown.

We used Biostator in >250 glucose clamps within the last 3 yr. During clamp experiments, it also facilitates remote control and after experiments allows immediate data analysis. Therefore, data files were read by a conventional spread-sheet program that could read and convert ASCII format, and all calculations and graphical presentations were done with this program (4,5).

Biostator runs on any IBM compatible personal computer with a standard serial port. Because no graphics are produced during the data acquisition, problems with different graphic standards do not occur. A copy of the program with the documented source file and a short manual is available on request.

References

1. DeFronzo RA, Tobin JD, Andres R: Glucose clamp technique: a method for quantifying insulin secretion and resistance. *Am J Physiol* 6:E214–24, 1979
2. Ponchner M, Heine RJ, Pernet A, Hanning I, Francis AJ, Cook D, Orskow H, Alberti KGMM: A comparison of the artificial pancreas (glucose controlled insulin infusion system) and a manual technique for assessing insulin sensitivity during euglycaemic clamping. *Diabetologia* 26:420–25, 1984
3. Clemens AH, Hough DL, Orazio PA: Development of the Biostator glucose clamp algorithm. *Clin Chem* 28:1899–904, 1982
4. Starke AAR, Heinemann L, Hohmann A, Berger M: The action profiles of human NPH insulin preparations. *Diabetic Med* 6:239–44, 1989
5. Heinemann L, Starke AAR, Heding L, Jensen I, Berger M: Action profiles of fast onset insulin analogues. *Diabetologia* 33: 384–86, 1990
6. Matthews DR, Hosker JP: Unbiased and flexible iterative computer program to achieve glucose clamping. *Diabetes Care* 12:156–59, 1989

Reduction of Hyperinsulinemia by Glyburide—Scientific Fact or Advertising Fiction?

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A recent advertisement, published in *Diabetes Care* and other major medical journals, promotes Diabeta (glyburide) as a drug that produces "glycemic control without the risks of hyperinsulinemia." A single article from 1971 is referenced to prove this point (1). Seven patients were given varying dosages of glyburide and after 2 mo fasting and stimulated (i.e., after an oral glucose challenge) insulin levels were significantly increased. At 6 mo, fasting insulin levels had returned to baseline (i.e., before drug) levels and stimulated insulin concentrations had decreased to levels that were still higher but not statistically different from baseline.

In contrast, most of the data in the literature demonstrate that chronic use of glyburide results in statistically significant increases in stimulated (i.e., after meals or oral glucose) insulin concentrations. We found 15 articles in which stimulated-insulin concentrations were measured before and after at least 6 wk (range 6–60 wk) of glyburide therapy. In four (1–4), stimulated-insulin levels after chronic glyburide use were not statistically different from baseline. On the other hand, in 11 reports (5–15), stimulated-insulin levels were significantly elevated after chronic glyburide therapy compared to baseline. Thus, 11

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of 15 studies do not support the contention put forward in the advertisement.

In many of these studies, increased insulin levels were associated with marked improvement in glycemic control. This contradicts the theory that those who respond are less likely to show hyperinsulinemia because their lowered glucose levels would stimulate the β-cell less. However, in most articles, responders and nonresponders were not separated and, therefore, this possibility could not be examined in detail. On the other hand, hyperinsulinemia after chronic glyburide therapy is consistent with the glucose toxicity theory, which holds that hyperglycemia suppresses β-cell function and lowered glucose levels restores it, at least partially (16).

Although advertisements are not subject to scientific review, we feel that it is important to present accurate scientific information under all circumstances. Due to the nature of clinical research and the publication of studies that often yield conflicting results, data are often available to support diverse claims. Only through a careful review of the literature can accurate conclusions be drawn. We do not recommend using glyburide over another sulfonylurea agent for the express purpose of lower serum-insulin levels. Although this may be an attractive goal, available scientific evidence does not support this as an effect of the chronic use of glyburide (or other sulfonylurea agents) in most patients. On the other hand, we frequently prescribe glyburide for our non-insulin-dependent diabetic patients.

References

1. Feldman JM, Lebovitz HE: Endocrine and metabolic effects of glybenclamide. *Diabetes* 20:745–55, 1971
2. Herrold JN, Tzagournis M, Skillman TG: Acute and chronic studies using a new oral hypoglycemic agent, glyburide. *Metabolism* 20:414–21, 1971
3. Duckworth WC, Solomon SS, Kitabchi AE: Effect of chronic sulfonylurea therapy on plasma insulin and proinsulin levels. *J Clin Endocrinol Metab* 35:585–91, 1972
4. Prosser PR, Kosola JW, Bowers CY: The 24-hour effects of glyburide and chlorpropamide after chronic treatment of type II diabetic patients. *Amer J Med Sci* 289:179–85, 1985
5. Chandalia HB, Hollobaugh SL, Pennington LF, Boshell BR: Use of glibenclamide in maturity onset diabetes—effect of the drug on serum insulin levels. *Horm Metab Res* 1 (Suppl. 1):73–76, 1969
6. Anderson J, Coulson RR, Grassick BDM, Morris BA, Thomas WD, Tomlinson RWS, Woodroffe F: Clinical and metabolic study in diabetic patients treated with glibenclamide. *Br Med J* 2:568–70, 1970
7. Defronzo RA, Simonson DC: Oral sulfonylurea agents suppress hepatic glucose production in non-insulin-dependent diabetic individuals. *Diabetes Care* 7 (Suppl. 1):72–80, 1984
8. Kolterman OG, Gray RS, Shapiro G, Scarlett JA, Griffin J, Olefsky JM: The acute and chronic effects of sulfonylurea therapy in type II diabetic subjects. *Diabetes* 33:346–54, 1984
9. Owens DR: Effects of sulfonylureas on the spectrum of defects in non-insulin-dependent diabetes mellitus. *Am J Med* 79(Suppl 2B):27–32, 1985
10. Hughes TA, Kramer JO, Segrest JP: Effects of glyburide therapy on lipoproteins in non-insulin-dependent diabetes mellitus. *Am J Med* 79(Suppl 3B):86–91, 1985
11. Groop L, Groop P-H, Stenman S, Saloranta C, Totterman KJ, Fyhrquist F, Melander A: Comparison of pharmcokinetics, metabolic effects and mechanisms of action of glyburide and glipizide during long-term treatment. *Diabetes Care* 10: 671–78, 1987
12. Hother-Nielsen O, Schmitz O, Anderson PH, Pederson O, Beck-Nielsen H: In vivo action of glibenclamide in obese subjects with mild type 2 (non-insulin dependent) diabetes. *Diabetes Res* 8:63–70, 1988
13. Jeng CY, Hollenbeck CB, Wu MS, Chen YDI, Reaven GM: How does glibenclamide lower plasma glucose concentration in patients with type 2 diabetes? *Diabetic Med* 6:303–308, 1989
14. Shapiro ET, Cauter EV, Tillil H, Given BD, Hirsch L, Beebe C, Rubenstein AH, Polonsky KS: Glyburide enhances the responsiveness of the β-cell to glucose but does not correct the abnormal patterns of insulin secretion in noninsulin-dependent diabetes mellitus. *J Clin Endocrinol Metab* 69:571–76, 1989
15. Nyomba BL, Freymond D, Raz I, Stone K, Mott DM, Bogardus C: Skeletal muscle glycogen synthase activity in subjects with non-insulin-dependent diabetes mellitus after glyburide therapy. *Metabolism* 39:1204–10, 1990
16. Unger RIT, Grundy S: Hyperglycaemia as an inducer as well as a consequence of impaired islet cell function and insulin resistance: implications for the management of diabetes. *Diabetologia* 28:119–21, 1985