Data Transfer From Biostator

Facilitation of Analysis of Glucose-Clamp Experiments

LUTZ HEINEMANN, DIPL BIOL DIPL LUG
KLAUS KAMPER, DIPL BIOL
WERNER KUNZE, MD

Glucose clamps can be performed manually (1) or with a glucose-controlled insulin infusion system (Biostator, Life Science, Miles, Indiana, USA) (2). To achieve a tight clamp at the desired blood glucose concentration, special clamp algorithms have been developed (3) and implemented into the Biostator as mode 9. Production of the Biostator has been withdrawn but still is an important tool for diabetes research. We use it extensively for glucose clamps during pharmacokinetic studies (4,5). The computer in the Biostator was a state-of-the-art computer during its development, but no data storage was supported. Therefore, for analysis of the data, we routinely transferred data via keyboard into a computer. To avoid this cumbersome work, we developed a data acquisition program that receives the data sent by the Biostator. The program filters the values of requested variables from the transmitted data, shows these values on the screen, and stores them. To our knowledge, no other program developed for this purpose has been published, whereas, some other programs and algorithms for glucose clamps have been described (6).

The Biostator has a serial port (EIA card) that uses the RS-232-C specification.The data transfer rate is 110 baud with one start bit, eight data bits, two stop bits, and no parity bits. No communication control (hand shaking) is supported by the Biostator. Characters are transmitted in ASCII 7 bit code and their sequence is exactly the same as those printed each minute by the Biostator. In the clamp mode, 9:1 values of the following variables are transmitted: *1*) number of days since the Biostator was started, 2) actual time, 3) actual blood glucose concentration, *4*) amount of glucose to be infused in the next minute, *5*) summed amount of total infused glucose, *6*) amount of insulin to be infused in the next minute, *7*) summed amount of total infused insulin, and *8*) a glucose utilization factor calculated by the Biostator with a simple formula. Serial ports of many personal computers also use the RS-232-C specification. Our program initializes the serial port so that no additional hardware is required beside the normal serial cable and a conventional null modem to establish communication between both machines.

At first, the program, which was written in Turbo Pascal 5.0 (Borland, Munich, Germany), configurates the serial port with appropriate settings. After a starting procedure, during which some informations have to be fed in, data from the Biostator can be received and filtered. A selection of requested values is then shown on the computer monitor and subsequently stored on hard disk. No further on-line analysis or graphical presentation of the gathered data is implemented. Because all communication with the Biostator has to be done by answering printed messages via a simple keyboard, a complex analysis of transmitted data has to be performed to select the desired values. From the sequence of variables transmitted each minute, the following variables were selected: time, blood glucose concentrations, glucose infusion rates, and glucose utilization factor. If the Biostator detects an error or if the machine is set in the *hold* modus, differences in the sequence of values transmitted occur. Events like this are adequately handled by the program. During the start procedure, a file name must be chosen for subsequent data storage. Selected data are stored as ASCII characters in a data file with the suffix ".ASC" to the file name. For additional analysis, all signs transmitted by the Biostator are stored in a file with the suffix ".BAK." The content of this file is identical with the Biostator print out. Data are stored every minute immediately after their reception to enhance data security in case of a system failure.

If the Biostator signals an error, the computer also gives an alarm, depending on the "short" or "long" selection for 3 or 30 s. Upper and lower limits at which additional warnings are given can be chosen. When inputs of the start procedure are confirmed, connection between both machines is established, and transmitted data can be received and analyzed. Selected values are shown on the left half of the screen, a new line for every minute. The values of the last 20 min are shown on the screen. If the blood glucose value exceeds the upper or lower limit, an alarm is given, values in this line are shown darker, and a "<" or

FROM THE DEPARTMENT OF NUTRITION AND METABOLIC DISEASES, WORLD HEALTH ORGANIZATION COLLABORATING CENTER FOR DIABETES, HEINRICH-HEINE-UNIVERSITY, DÜSSELDORF, GERMANY.

ADDRESS CORRESPONDENCE AND REPRINT REQUESTS TO LUTZ HEINEMANN, DIPL BIOL DIPL LUG, ABTEILUNG ERNÄHRUNG UND STOFFWECHSEL, HEINRICH-HEINE-UNIVERSITÄT DÜSSELDORF, MOORENSTR. 5, 4000 DÜSSELDORF 1, GERMANY.

RECEIVED FOR PUBLICATION 9 DECEMBER 1990 AND ACCEPTED IN REVISED FORM 6 MAY 1991.

">" 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?

ANNE L. PETERS, MD
MAYER B. DAVIDSON, MD

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

FROM CEDARS-SINAI MEDICAL CENTER, UCLA SCHOOL OF MEDICINE, LOS ANGELES, CALIFORNIA.

ADDRESS CORRESPONDENCE AND REPRINT REQUESTS TO MAYER B. DAVIDSON, MD, DIVISION OF ENDOCRINOLOGY, B-131, CEDARS SINAI MEDICAL CENTER, 8700 BEVERLY BLVD., LOS ANGELES, CA 90048.