Band 29 · Heft 4 April 1984

Biomedizinische Technik

Biomedical Engineering

Gemeinschaftsorgan der Deutschen*, der Österreichischen und der Schweizerischen Gesellschaft für Biomedizinische Technik

Publication of the German, Austrian and Swiss Association on Biomedical Engineering

Verlag/Publishing Company:

Fachverlag Schiele & Schön GmbH
Postfach 610280, Markgrafenstraße 11, D-1000 Berlin 61
Telefon-Sammel-Nr. 030/2516029
Telex 181470 sunds d

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Biomed. Technik
29 (1984), 62–66

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Simplified Evaluation and Documentation of Data from Glucose Controlled Insulin Infusion System (GCIIS)

Computerunterstützte Datenauswertung und Dokumentation beim Einsatz glukosekontrollierter Insulininfusionssysteme

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Key-words: Glucose controlled insulin infusion, artificial beta cell, data processing, metabolic control in diabetes mellitus

A computer-assisted method for complete processing of data from a glucose-controlled insulin infusion system (GCIIS) is demonstrated. All data are transferred directly from the GCIIS to a microcomputer by means of an interface. A BASIC computer programme has been developed for rapid calculation of mean blood glucose (MBG), an index of blood glucose control (M-value) and a measure of diabetic instability (MAGE) in order to assess the state of glycemic control. All GCIIS-data as well as calculated parameters are stored on floppy disks and can be recorded by a printer-plotter immediately after the GCIIS control period. The device is particularly useful for optimizing conventional subcutaneous insulin therapy by means of a GCIIS.

Schlüsselwörter: Glukosegesteuerte Insulin-Infusion, künstliche Beta-Zelle, Meßdatenverarbeitung, Stoffwechselüberwachung beim Diabetes mellitus

Eine computerunterstützte Methode zur vollständigen Datenverarbeitung beim Einsatz glukosekontrollierter Insulininfusionssysteme (GCIIS) wird vorgestellt. Mit Hilfe eines Interface werden alle Daten direkt vom GCIIS auf einen Mikrocomputer übertragen. Ein BASIC-Computerprogramm wurde für die schnelle Berechnung von Kenngrößen des Glukosestoffwechsels (mittlerer Blutzucker, M-value als Index für die Blutzuckerkontrolle und MAGE als Maß für Blutzuckerschwankungen) entwickelt. Sämtliche GCIIS-Daten werden ebenso wie berechnete Parameter und Klartextkommentare auf Floppy-Disks gespeichert und können von einem Printer-Plotter ausgedruckt werden. Die Methode erlaubt eine vollständige Verarbeitung sämtlicher GCIIS-Daten am Krankenbett; sie hat sich z. B. zur Überprüfung und Verbesserung der Stoffwechselkontrolle unter konventioneller subcutaner Insulin-Therapie bewährt.

Introduction

Three parameters for assessment of metabolic control in diabetic patients commonly used are: 1) the diurnal mean blood glucose concentration (MBG), 2) the so-called M-value [11], the logarithmic transformation of the deviation of glycemia from an arbitrarily selected standard, and 3) MAGE [13] the mean amplitude of glycemic excursions. When applied to a few blood glucose values at selected time points during the course of the day, conventional mathematical evaluation of these parameters may be feasible. However, this is almost impossible during the use of a glucose controlled insulin infusion system (GCIIS). Complete processing of GCIIS-data would require the time-consuming keybord entry of a vast number of values into a calculator. For this reason, an interface between the GCIIS and a microcomputer has been employed to transfer all data directly at one minute intervals. Further, a BASIC computer programme has been developed for rapid calculation of MBG, M-value and MAGE. Our bed-side method permits the complete processing and recording of GCIIS-data.

Materials and methods

A schematic diagram of the technical equipment is shown in figure 1. The patient is connected to the GCIIS (Biostator Controller, Life Science Instruments, Miles Laboratories, Elkhart, USA), the details of which have been described elsewhere [3, 4, 8]. By means of an interface all data for blood glucose concentration (BG), insulin infusion rate (IR) and dextrose infusion rate (DR) are transferred directly from the GCIIS to a microcomputer (PC 800, Magirus Datentechnik, Leinfelden-Echterdingen, West Germany) for further processing. The microcomputer provides the following functions (figure 1):

1) Monitoring: BG, IR and DR are plotted continuously.
2) Manual input: comments concerning e.g. the actual therapy can be entered via keybord.
3) Calculations: a BASIC computer programme has been developed for the calculation of
   - $\text{MBG (mg/dl)} = \frac{1}{n} \sum_{1}^{n} \text{BG}$

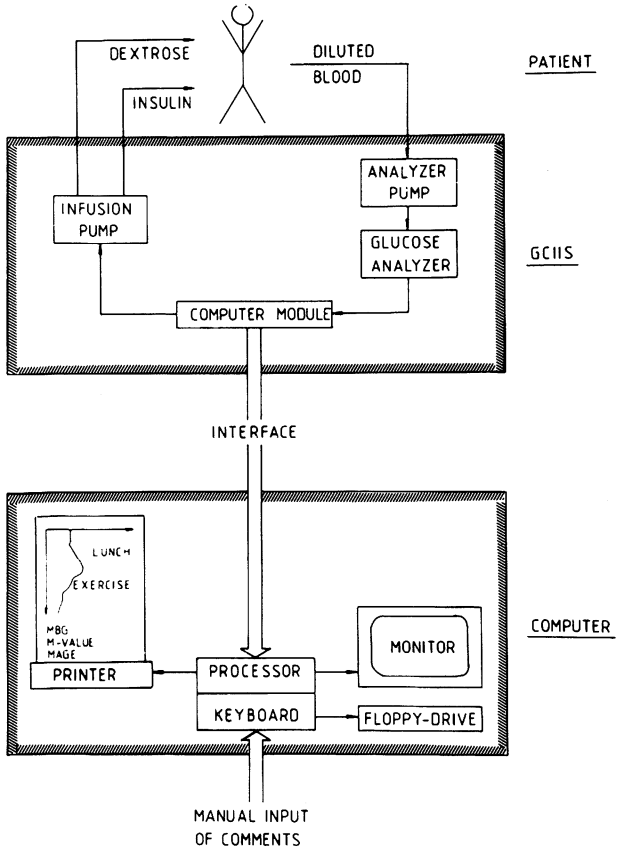

Figure 1. Schematic diagram of device used for processing of GCIIS-data.

M-value: The M-value is a quantitative index of the deviation of several blood glucose (BG) determinations in a twenty-four-hour period from an arbitrarily selected standard (120 mg/dl). The mathematical formula was designed to give proportionately greater emphasis to hypoglycemia than to hyperglycemia:

$$\text{M-value} = \frac{1}{n}\sum_{1}^{n}\left(10 \log \frac{BG}{120\ \text{mg/dl}}\right)^3 + \frac{BG_{max} - BG_{min}}{20\ \text{mg/dl}}$$

MAGE: The calculation of MAGE is based on a logical algorithm (figure 2). It is defined as the arithmetic mean of those glycemic excursions which satisfy the following conditions:

1. The excursion (from blood glucose nadirs to peaks or vice versa) must exceed one standard deviation of the mean blood glucose of the same twenty-four-hour period.
2. The succeding excursion in opposite direction (peak to nadir or vice versa) must also exceed one standard deviation.
3. The excursion must have the same direction as the *first* excursion which exceeds one standard deviation and thus establishes the direction of calculation.

4) Printer and Floppy Discs: All values for BG, IR, DR as well as comments which appear in their time-related positions, and calculated parameters are plotted and documented on 5 inch floppy discs.

The BASIC-programme may be obtained by interested investigators from the authors upon writing.

Results

Figures 3 and 4 show as an *example* the data obtained from an insulin-dependent diabetic patient treated by a combination of. s.c. insulin injections and feedback control by the GCIIS. The first control period shows the assessment of additional insulin requirements for optimizing metabolic control. The patient received intermediate insulin, 28 U in the morning and 16 U in the evening. The total amount of insulin given in addition by the GCIIS for feedback control was 24.3 U regular insulin. Insulin requirements were highest after breakfast, lunch and evening snack. There was a tendency towards hypoglycemia during midnight, which was counterregulated by 7.7 g dextrose administered. According to these data the patient was placed on a new insulin regimen: 22 U intermediate plus 6 U regular insulin in the morning and 18 U intermediate insulin in the evening. A second control period six weeks later clearly showed improved metabolic control. The additional amount of insulin given by the GCIIS was reduced to 4.7 U. There was only a slight tendency towards hypoglycemia during the night. Table 1 shows the parameters for metabolic control calculated for the two GCIIS runs using all data obtained from the system.

Table 1. Parameters reflecting metabolic control calculated by complete evaluation of the two GCIIS runs.

	Run 1	Run 2
MBG±SD (mg/100 ml)	120±35	101±20
M-value	14	7
MAGE (mg/100 ml)	72	53
Number of excursions	5	4

Discussion

Glucose controlled insulin infusion systems have been successfully used to determine insulin requirements for conventional subcutaneous insulin therapy [1, 6, 9, 10] and for continuous subcutaneous or intravenous insulin infusion with portable pumps [5, 14]. In order to assess the state of glycemic control, three parameters are commonly used: MGB, the mean of all blood glucose values; the M-value, a parameter indicating the

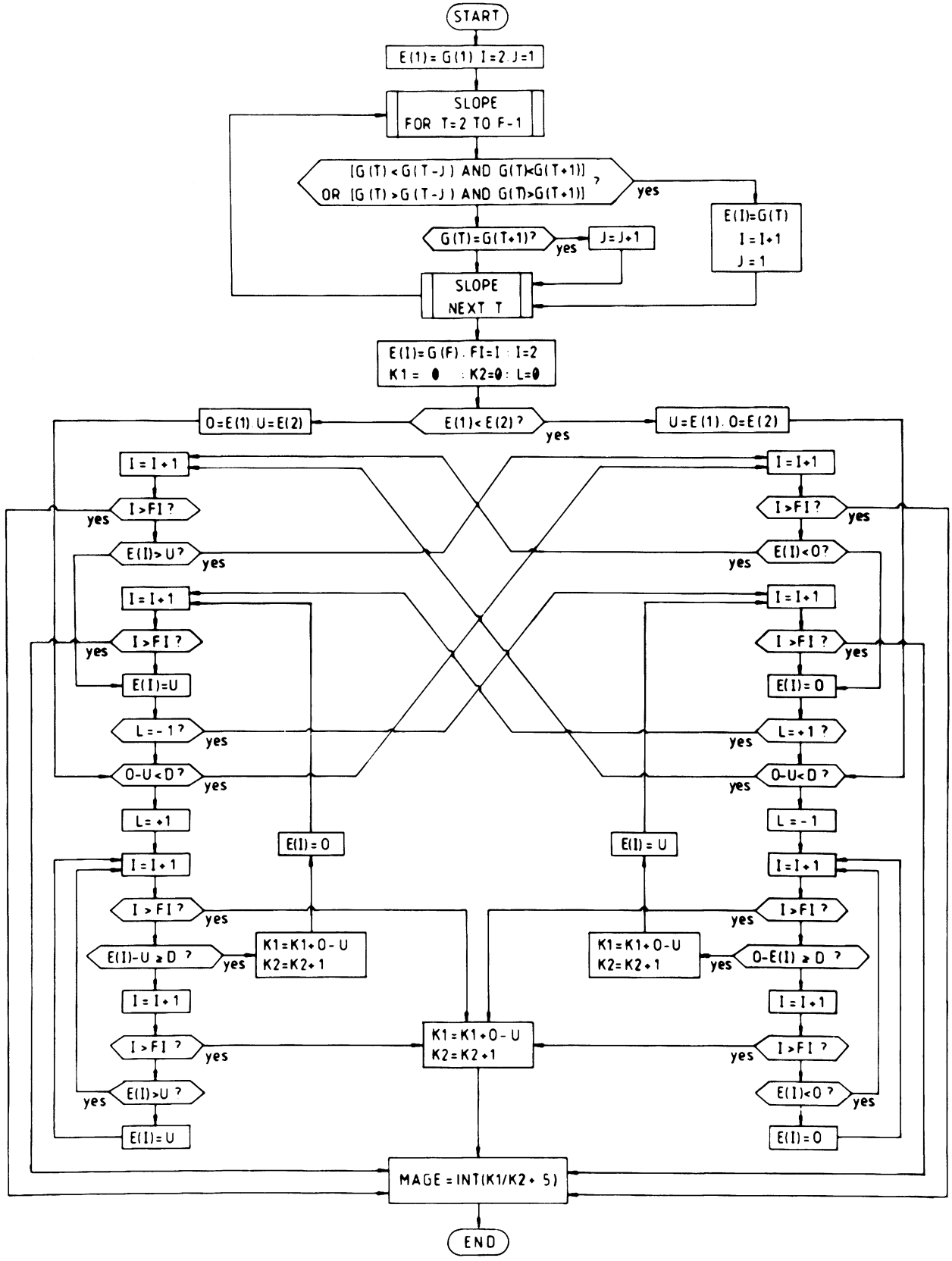

Figure 2. Flow diagram for calculation of MAGE.
Abbreviations: G (T) = blood glucose level at time T; E (I) = blood glucose level of the I-th relative extreme; F = number of measurements (T from 1 to F); FI = number of relative extrema (I from 1 to FI); J = duration of stationary relative extrema; L = indicates, whether all excursions are counted in peak-to-nadir (L = −1) or in nadir-to-peak direction (L = +1); D = standard deviation; O, U = greatest relative maximum (O) and smallest relative minimum (U) during an interval. These values are tested according to the criteria for counted excursions; K_1 = total of excursions counted for MAGE; K_2 = number of excursions counted for MAGE.

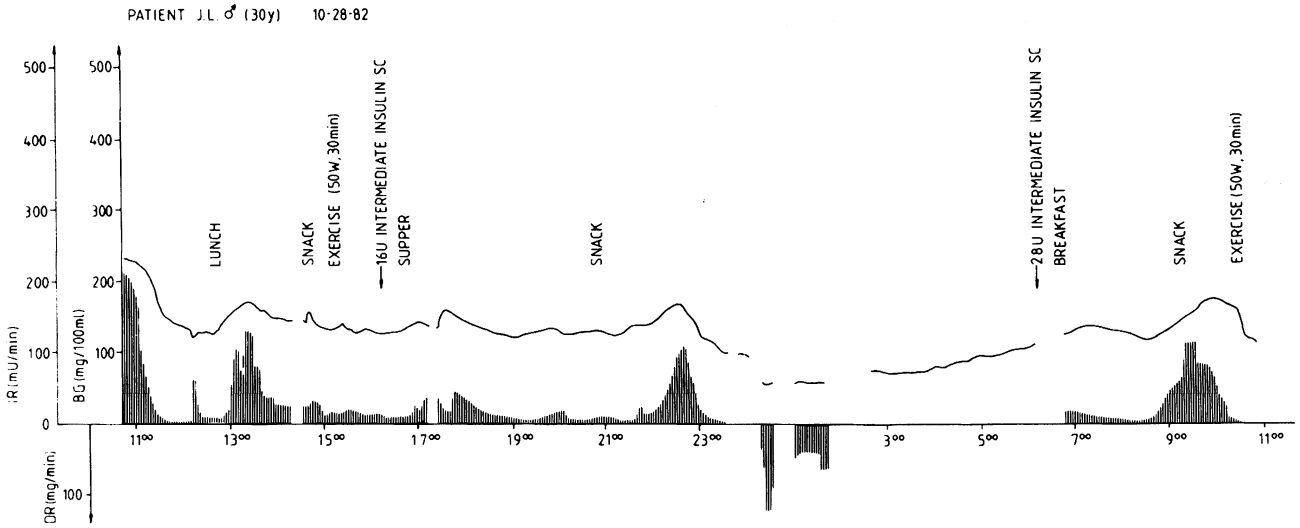

Figure 3. Blood glucose (BG), insulin infusion rates (IR) and dextrose infusion rates (DR) in a diabetic patient on conventional s.c. insulin therapy during a 24-hour feedback control by the GCIIS. Constants: VAR 100, BI 130, FI 325, RD 25, BD 65, FD 240. Assessment of additional insulin requirements for optimizing s.c. therapy.

duration and the degree of pathological blood glucose values, and MAGE, the mean amplitude of glycemic excursions, a measure of diabetic instability.

The results of this study offe the possibility to calculate on the basis of minute to minute blood glucose measurements these parameters more exactly than at selected time points, as suggested by others [7]. In particular, the computer programme and the technical equipment employed have the following advantages:

MGB, M-value and MAGE can be calculated immediately after the end of a GCIIS control period. To our knowledge, rapid calculation of MAGE from GCIIS-data by means of a specific BASIC-computer programme using a micro-computer has not been reported up to now. In 1982, Brunetti et al. [2] for the first time presented a computerized system for evaluation and documentation of GCIIS-data. However, the concept of these authors required data transmission from a mini-computer to a computer center for mathematical and statistical analysis. Therefore, evaluation of metabolic parameters such as MAGE could not be performed as a bedside method. – Further, all data from each patient during a control period are stored on a floppy disc and can be printed at any time. This is of particular interest for evaluating and comparing treatment regimes during extended periods.

Figures 3 and 4 illustrate the usefulness of our method for the improvement of therapy in a diabetic on conventional subcutaneous insulin regimen. Obviously, the procedure can be applied likewise in order to determine the insulin requirements and the state of metabolic

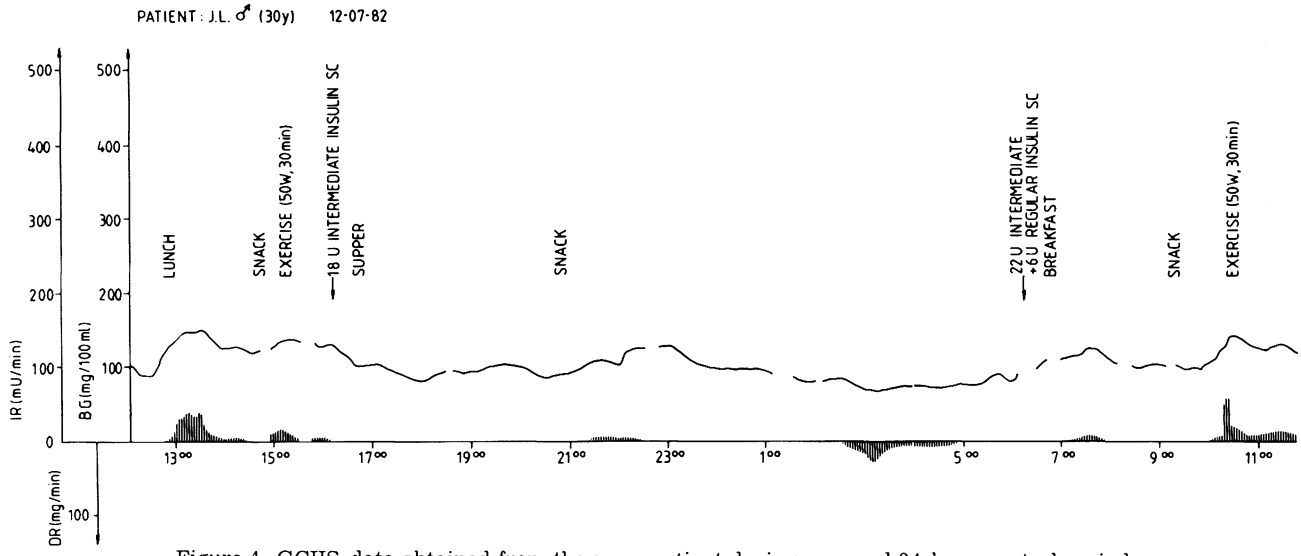

Figure 4. GCIIS-data obtained from the same patient during a second 24-hour control period six weeks later. New insulin regimen calculated according to the data from the first GCIIS-run. Improved metabolic control.

control in preprogrammed insulin infusion therapy. Finally, the method is not confined to routine clinical management of diabetes mellitus. It can also be recommended in critical care medicine. Preliminary results [12] have proved its usefulness in evaluating the metabolic therapy with glucose-insulin-potassium infusions guided by a GCIIS in patients with acute myocardial infarction.

References:

[1] Beyer, J., G. Becker, G. Schulz, E. Gaberle, E. Wolf, W. Hassinger, U. Cordes: Blutzuckerkontrollierte Insulin-Infusionssysteme zur Schnelleinstellung insulinpflichtiger Diabetiker. Dtsch. med. Wschr. 106 (1981), 1644–1649

[2] Brunetti, P., G. Calabrese, G. Cecconi, M. Massi-Benedetti, A. Bueti, F. Santeusanio, F. Landi, G. Bellomo: Computerized system for the analysis of blood glucose regulation and beta cell function stimulation: application in a closed-loop system (Biostator, GCIIS). Horm. Metab. Res. Suppl. 12 (1982), 179–183

[3] Clemens, A. H., P. H. Chang, R. W. Myers: The development of Biostator, a glucose controlled insulin infusion system (GCIIS). Horm. Metab. Res. Suppl. 7 (1978), 23–33

[4] Fogt, E. J., L. M. Dodd, E. M. Jenning, A. H. Clemens: Development and evaluation of a glucose analyzer for a glucose-controlled insulin infusion system (Biostator). Clin. Chem. 24 (1978), 1366–1372

[5] Kølendorf, K., J. S. Christiansen, J. Bojsen, P. A. Svendsen, L. L. S. Teglbjaerg: Determination of 24-hour insulin infusion pattern by an artificial endocrine pancreas for intravenous insulin infusion with a miniature pump. Horm. Metab. Res. 13 (1980), 245–249

[6] Lambert, A. E., M. Buysschaert, E. Marchand, M. Pierard, S. Wojcik, L. Lambotte: Determination of insulin requirements in brittle diabetic patients by the artificial pancreas. Diabetes 27 (1978), 825–833

[7] Molnar, G. D., W. F. Taylor, A. Langworthy: On measuring the adequacy of diabetes regulation: comparison of continuously monitored blood glucose patterns with values at selected time points. Diabetologia 10 (1974), 139–143

[8] Pfeiffer, E. F., Ch. Thum, A. H. Clemens: The artificial beta-cell – a continuous control of blood sugar by exter- regulation of insulin infusion – (glucose controlled insulin infusion system). Horm. Metab. Res. 6 (1974), 339–342

[9] Ratzmann, K. P., W. Bruns, B. Schulz, E. Zander: Use of the artificial B-cell (Biostator) in improving insulin therapy in unstable insulin-dependent diabetes. Diabetes Care 5 (1982), 11–17

[10] Rizza, R. A., J. E. Gerich, M. W. Haymond, R. E. Westland, L. D. Hall, A. H. Clemens, F. J. Service: Control of blood sugar in insulin-dependent diabetes: comparison of an artificial endocrine pancreas, continuous subcutaneous insulin infusion, and intensified conventional insulin therapy. N. Engl. J. Med. 303 (1980), 1313–1318

[11] Schlichtkrull, J., O. Munck, M. Jersild: The M-value, an index of blood sugar control in diabetics. Acta Med. Scand. 177 (1965), 95–102

[12] Scriba, P. C., H. Djonlagic, G. Müller-Esch: Endokrines System und Schock. Internist 23 (1982), 433–440

[13] Service, F. J., G. D. Molnar, J. W. Rosevear, E. Ackermann, L. C. Gatewood, W. F. Taylor: Mean amplitude of glycemic excursions, a measure of diabetic instability. Diabetes 19 (1970), 644–655

[14] Service, F. J., R. A. Rizza, R. E. Westland, L. D. Hall, R. L. Nelson, M. W. Haymond, A. H. Clemens, J. E. Gerich: Considerations for the programming of an open-loop insulin infusion device from the Biostator glucose controller. Diabetes Care 3 (1980), 278–284

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