Experience with the Internet Release of AIDA v4.0
- http://www.diabetic.org.uk/aida.htm -
An Interactive Educational Diabetes Simulator

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ABSTRACT

AIDA v4.0 is a freeware computer program that permits the interactive simulation of plasma insulin and blood glucose profiles for demonstration and teaching purposes. It has been made freely available, without charge, on the World Wide Web as a noncommercial contribution to continuing diabetes education. Since its Internet launch in 1996 over 23,000 people have visited the AIDA Web site (http://www.diabetic.org.uk/aida.htm) and over 7,750 copies of the program have been downloaded gratis. This report overviews the Internet release of AIDA v4.0 and provides examples of the simulator in operation. The concept of a “virtual diabetic patient” is introduced. This provides an electronic representation of a patient with diabetes that can be used for self-learning/teaching/demonstration purposes.

INTRODUCTION

THERE IS GROWING INTEREST in the application of information technology in clinical diabetes care.1 The rationale underlying this interest is the hope that computer systems may offer a way of improving the therapy offered to patients with diabetes thus permitting more patients to be managed more intensively, in line with the experience of the Diabetes Control and Complications Trial.2 In addition to database systems and decision support prototypes,3 an area of clinical diabetes care in which computers may have a great deal to offer is education.4–6

There are many different aspects to diabetes education, but learning facts is only one of these. The ability to gain experience is also of great importance. It is well recognized that it is not ideal for patients to learn about diabetes control solely from real-life experiences because of the long time frames involved, aside from the possible very real dangers of hypoglycemia or hyperglycemia. For this reason, it has been suggested that an interactive simulation of a diabetic patient might offer one solution.7 In the same way that aircraft pilots and air traffic controllers are trained on airplane and air traffic simulators, it should be possible for diabetic patients and health care students to be trained to make appropriate responses to everyday situations on a diabetes simulator.8 While other interactive simulators of glucose-insulin interaction have been described in the literature,9–12 to date none of these have been distributed widely via the Internet.
AIDA v4.0 is a diabetes simulator that can be used for demonstration and teaching purposes to simulate the effects of changes in insulin therapy and diet on the blood glucose (BG) profile.\textsuperscript{13} The AIDA software can be downloaded without charge from the World Wide Web\textsuperscript{14} where it is being made freely available, as a noncommercial contribution to continuing diabetes education (Fig. 1).\textsuperscript{15} A version of the program, on diskette, with a printed, bound manual is also available to health-care professionals in the United Kingdom from the British Diabetic Association (London, UK).\textsuperscript{16,17}

The AIDA system incorporates a compartmental model that describes glucose-insulin interaction in patients completely lacking endogenous insulin secretion. It contains a single extracellular glucose compartment into which glucose enters via both intestinal absorption and hepatic glucose production. The AIDA model also contains separate compartments for plasma and “active” insulin,\textsuperscript{9} the latter being responsible for glycemic control while insulin is removed from the former by hepatic degradation. Figure 2 summarizes the compartmental structure of the model,\textsuperscript{18} the mathematics of which have been described elsewhere.\textsuperscript{19} Full details of the AIDA model are also accessible from within the AIDA software package, and can be viewed and printed separately from the Internet.\textsuperscript{20} Table 1 summarizes the main classification and pharmacodynamic details of insulin preparations catered for in AIDA v4.0.\textsuperscript{7}

The clinical application of an interactive educational simulator like AIDA requires users to know what they wish to try simulating next. In practice, certainly for use by patients, such knowledge cannot be assumed. For this reason a simple knowledge-based system has been provided within AIDA to identify possi-
FIG. 2. Anatomic basis and physiological functions of the AIDA model. GAR, glucose absorption rate; cho, carbohydrate; NHGB, net hepatic glucose balance; RBC, red blood cell; IIGU, insulin-independent glucose utilization; AG, arterial plasma glucose; PGU, peripheral glucose utilization; BG, blood glucose; UGER, urinary glucose excretion rate. (Modified from Lehmann and Deutsch.)
ble problems that might require remedy. A list of suggestions that might correct some of these problems can also be generated as a prompt to the sort of insulin dosage adjustments that users might like to try simulating. The interactive application of this knowledge-based system linked to the compartmental model provides educational opportunities that might otherwise not be available to patients, their relatives, students, or even health care professionals using the software on their own.

It is important to note that AIDA, like other model-based approaches, is not sufficiently accurate to be used for individual patient simulation or glycemic prediction. Therefore, as the program makes clear, it is not intended for therapy planning and can only be used for teaching/self-learning or demonstration purposes.

AIDA CASE STUDY

The AIDA software comes with 40 educational case scenarios as standard, each of which represents a snapshot of the metabolic status of a typical patient with respect to diabetes mel-
EXPERIENCE WITH AIDA v4.0

posed on these graphs are predicted steady-state BG and plasma insulin profiles as calculated by the AIDA model after parameter estimation.19

Having performed this baseline simulation, users can change any of the input variables shown on the AIDA data entry screen to simulate the glycemic effects of such changes. For example, a user could simulate what would happen to a hypothetical patient’s BG profile if the bedtime Humulin I dose was increased by 2 units, or the injection time moved later, or the bedtime snack shifted earlier, or the carbohydrate content of supper decreased by 10 g. A user could transfer the patient to Humulin M3 in place of the previous short- and intermediate-acting preparations, or perhaps try the case scenario with a “pen regimen” taking a longer-acting insulin preparation at night. The list of possibilities is endless—a near infinite number of simulations can be performed with AIDA.

As can be seen in Figures 3A and 3B, Ian, our virtual diabetic patient, experienced a hypoglycemic episode at 9:30 AM. Figure 4A shows the effect on the BG profile of changing the 6:30 AM breakfast insulin injection from 10 units of Humulin S to 4 units of Humulin S and 3 units of Humulin I. While this does not fully control the evening BG level, the morning dip in BG is corrected. However, supposing that because of the 9:30 AM “hypo” Ian decided to leave off his 12 PM injection of 6 units of Humulin S. This situation can also be simulated with AIDA. Figure 4B shows the hyperglycemia that would result in the afternoon/evening with a peak BG of 323 mg/dL (17.9 mmol/L) predicted at 6 PM (18:00 hours).

If the user is not quite sure how to correct the 9:30 AM “hypo”—a knowledge-based system built into AIDA can also be used to identify potential problems in the case scenario’s “observed” BG profile, and suggest various solutions that might be worth simulating.18 Figure 4C shows the knowledge-based system’s suggestions for Ian’s original baseline case scenario data (given in Fig. 3A). In this example the user has interactively selected on the right of the screen to simulate the glycemic effect of both suggestions, to decrease the morning Humulin S dose and the bedtime Humulin I dose. Figure 4D shows the effects of these changes being simulated. As can be seen, this raises Ian’s BG profile during the course of the day, with the lowest BG level now being 61 mg/dL (3.4 mmol/L) at 10:15 AM.

However, Ian still tends to have high BG levels in the afternoon/evening. Figure 5A shows how AIDA can be used to simulate a completely new insulin regimen. In this case, Ian’s carbohydrate intake remains the same, but instead of 4 injections per day, he is switched to 3 injections of 10 units of premixed (biphasic) insulin (Mixtard 30/70), with a substantial improvement in day-long glycemic control (a user definable normoglycemic range of 72–180 mg/dL [4–10 mmol/L] is shown superimposed). However, Figure 5B shows the low BG that would result if Ian took his lunchtime insulin injection but missed lunch. He would be at risk of a “hypo” in the early afternoon with a BG of approximately 50 mg/dL (2.8 mmol/L) predicted at 2:15 PM (14:15 hours).

It is also possible to use AIDA to gain a deeper insight into the way glucose is handled in these simulations. Figure 5C demonstrates the different glucose fluxes for Ian Jones’ baseline Mixtard simulation (shown in Fig. 5A). The light blue “nhgb” curve represents the grouped peripheral, central nervous system, and red blood cell utilization of glucose; the purple “renal” curve is the net hepatic glucose balance (the production or utilization of glucose by the liver); the red “glucose absorption” curve is the systemic appearance of glucose from the gut; and the yellow “renal excretion” curve is the loss of glucose via the kidneys into the urine. In this case, as the BG level has been well controlled throughout the day, no renal excretion of glucose is seen.

At 2:15 PM (14:15 hours) glucose absorption from the gut peaks at over 1800 mg/h after the ingestion of 40 g of carbohydrate at lunch. However this peak is well covered by the Mixtard 30/70 injection taken just before lunch, so the BG profile during this time does not rise. Although this display may appear complicated, more user-friendly views of such data are feasible, and may potentially be of some use as a demonstration tool for teaching health care students about glucose homeostasis and carbohydrate metabolism in diabetes mellitus.

In addition to the examples shown above,
Data entry screen for AIDA v4.0 with clinical and nutritional data for a “virtual diabetic patient” (“Ian Jones”) who had a hypoglycemic episode at 9:30 AM. (B) Baseline simulation for Ian Jones using the insulin, dietary, and clinical data shown in Figure 3A. The upper panel shows blood glucose information while the lower panel represents a composite display of information regarding insulin and carbohydrate intake. The distribution of meals eaten can be seen in this panel along with the 4 times daily regular short-acting (Humulin S) and intermediate-acting (Humulin I) insulin regimen that was being used. The low blood glucose between 9:00 AM and 10:30 AM can clearly be seen. (AIDA can handle blood glucose data and display simulation results in both mg/dL and mmol/L.)
FIG. 4. (A) Demonstrates the effect on Ian Jones' blood glucose profile of changing his 6:30 AM insulin injection from 10 units of Humulin S to 4 units of Humulin S and 3 units of Humulin I. While this does not fully control the evening blood glucose level, the morning 'hypo' is corrected. The current blood glucose (BG) simulation is shown by the white line while the previous simulation is given by the thinner red line. (B) Demonstrates what would happen if Ian missed his 12:00 PM injection of 6 units of Humulin S because of his morning 'hypo'. The hyperglycemia that would result in the afternoon/evening is shown with a peak blood glucose of 323 mg/dL (17.9 mmol/L) predicted at 6:00 PM (18:00 hours). (C) Problems identified in Ian's BG profile and possible solutions (adjustments) suggested by the knowledge-based system are shown (for data from Figure 3A). Both suggestions have been selected interactively by the user. (D) Simulates the glycemic effect of the adjustments selected interactively in Figure 4C, decreasing both the 6:30 AM Humulin S dose and the 10:00 PM (22:00 hours) Humulin I dose from 10 to 7 units. An improvement in the morning BG profile results with Ian no longer being at such great risk of hypoglycemia. The lowest blood glucose level predicted is 61 mg/dL (3.4 mmol/L) at 10:15 AM.

Possible problems in the "observed" blood glucose data from the current scenario are shown along with insulin-dosage adjustments which may help improve glycemic control. You may like to try simulating the effects of some of these to see what happens to AIDA's blood glucose profile.

To select a piece of advice press the 'Y' key. (Default = No)

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<td>2</td>
<td>decrease dose of bedtime Humulin I</td>
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FIG. 5. (A) Simulates the effect of switching Ian Jones to a completely new insulin regimen. In this case he has been started on 10 units of Mixtard 30/70, a premixed (biphasic) preparation, injected 3 times per day at 6:00 AM, 11:30 AM, and 6:30 PM. A user-definable normoglycemic range (set at 72–180 mg/dL [4–10 mmol/L] is shown superimposed). (B) Demonstrates what would happen to Ian’s blood glucose profile if he were to take his 11:30 AM insulin injection but skip lunch. The AIDA model predicts that he would be at risk of hypoglycemia with a blood glucose of approximately 50 mg/dL (2.8 mmol/L) at 2:15 PM (14:15 hours). (C) Demonstrates, using the simulation shown in Figure 5A, how the different glucose fluxes within the AIDA model can be displayed for medical student teaching. See main text for explanation.
FIG. 6. Demonstration use of AIDA v4.0.
(A) Decreasing the dose of the before-breakfast Mixtard 30/70 injection from 10 units to 0, in 2-unit decrements. The resulting rise in the blood glucose profile can be clearly seen. (B) Increasing the carbohydrate content of the 10:00 AM midmorning snack from 20 g to 80 g in 10-g increments. The resulting rise in the blood glucose profile is clear. (C) Moving the 6:30 AM before-breakfast Humulin S injection to 7:30 AM in 15-minute increments. The rise in blood glucose that results from Ian Jones eating breakfast without cover from his usual insulin injection can be clearly seen.
**AIDA** can also be used to simulate a whole variety of “what if” type questions for demonstration purposes. Figure 6A uses Ian Jones’ baseline Mixtard simulation (from Fig. 5A) and demonstrates the effect on the BG profile of decreasing the before-breakfast insulin dose from 10 units to 0, in 2-unit decrements; the resulting rise in BG being clear to see. Dietary changes can also be simulated for educational purposes. Figure 6B reverts back to Ian Jones’ original 4 injections-per-day regimen (from Fig. 3B) and demonstrates the effect of increasing the carbohydrate intake. In this case the mid-morning snack has been raised from 20 g to 80 g in 10 g increments: the resulting rise in the BG profile being clear to see. Figure 6C illustrates a different principle—in this case the interaction between insulin and diet. Using the same baseline data as shown in Figure 6B the effect of shifting the early morning insulin injection time is simulated. In this case, the Humulin S injection is moved in 15-minute increments from 6:30 AM to 7:30 AM, while breakfast remains at 6:30 AM. As the Humulin S injection is administered later and later—due to breakfast not being covered by a short-acting insulin injection—a transient rise in the BG profile results. Appreciating this may be of some importance for patients who are trying to control their BG levels strictly.

Further examples of the use of the **AIDA** system as an educational tool can be found elsewhere in the literature, and a full demonstration can be viewed on-line or downloaded without charge from the **AIDA** Web site.**

**AIDA USAGE**

**AIDA** was released on the Internet for beta-testing in April 1996 and formally launched after user feedback in June 1996. In the 35 months until February 1999, there were over 23,000 visitors to the **AIDA** Web site (http://www.diabetic.org.uk/aida.htm). During this time, more than 7,750 full copies of the software (plus over 1,000 demonstration copies) were downloaded. The average number of visitors to the site rose from approximately 350 per month in 1996, to approximately 600 per month in 1997, and to more than 750 per month in the first 9 months of 1998. Figure 7 summarizes the number of visitors and downloads during the 30-month period between April 1996 and September 1998. Other Internet sites also store the **AIDA** software including the CompuServe Diabetes Forum, the CIX Balance (diabetes) archives, the Lehigh diabetes server, and the Diabetic DataCentre Web site. However, downloads from these satellite sites are not all counted or logged.

Over the 30 months from April 1996 to September 1998, registration forms and enquiries about **AIDA v4.0** were received from countries as far away as Australia, Turkey, The Netherlands, Poland, India, Japan, Canada, Italy, New Zealand, Portugal, Greece, Denmark, Malta, the Slovak Republic, Croatia, Switzerland, Sweden, Belgium, South Africa, Cyprus, Israel, Austria, Spain, Hungary, Portugal, France, Germany, Romania, Brazil, Finland, the Czech Republic, Colombia, Indonesia, Hong Kong, Chile, Estonia, China, Taiwan, Slovenia, Gibraltar, the United Kingdom and the United States. A range of user feedback about **AIDA** can be found on the Internet as well as elsewhere in the literature. However, another novel use of **AIDA** has been to support ongoing diabetes-computing research projects. For example, Belazzi and colleagues have described using simulated BG data from **AIDA** to test computer decision-support prototypes under development in their laboratory. Pender has reported using **AIDA** to provide BG data to train an artificial neural network (ANN) prototype, work that has since been taken forward in the same laboratory by Sandham and colleagues who have investigated making BG predictions using an ANN. Yates and Fletcher have investigated 3 models of the gut to assess how well they were able to predict the appearance of glucose after the ingestion of a carbohydrate meal. They found the **AIDA** model gave the best results, although it is recognized that carbohydrate content only forms 1 component of an ordinary meal.

Cobelli and colleagues are in the process of developing a new physiological model of glucose-insulin interaction in type 1 diabetes mellitus. This is intended to encompass newly acquired physiological knowledge about the time course of endogenous glucose production dur-
ing a meal,\textsuperscript{32} and about the effect of glucose and insulin signaling on glucose utilization,\textsuperscript{33} as well as apply more accurate descriptions of the action profiles of insulin after subcutaneous injection.\textsuperscript{34} As part of their testing procedure the researchers have been comparing the performance of their new model with other models of type 1 diabetes mellitus, including AIDA.\textsuperscript{31}

Various other research projects involving AIDA are ongoing, although these have not yet reported their results. Nevertheless, from its release to other researchers in 1995 and on the Internet in 1996, it is interesting to see how quickly such a simulation program can be adopted for wider research application. This should encourage more researchers to consider making use of the Internet for the distribution of their work. As in the case of AIDA, such distribution may not only possibly be of use to patients directly but may also actually help to promote further research. Publication of all AIDA model and systems details, as can be found both in the literature\textsuperscript{18,19} and on the Internet,\textsuperscript{20} may also help to support further research work in this field.

**DISCUSSION**

It is hoped that physiologically based simulators like AIDA may offer a useful tool for enhancing teaching of diabetic patients about how to modify their therapy on the basis of self-monitoring BG data. The idea is to allow patients or their relatives to use a "virtual diabetic patient" to experiment with various therapeutic options safe from the very great risks of hypoglycemia that would normally result from such real-life experimentation. The hypothesis underlying this approach is that through the use of such interactive software patient education may be enhanced, leading to an improvement in self-management and glycemic control. User feedback about AIDA from patients, their relatives, and health care professionals\textsuperscript{6,24} appears to support this concept. However, the hypothesis still needs to be formally tested in a prospective randomized controlled clinical trial.

Furthermore, the software does have certain limitations. At present the AIDA model does not contain representations for exercise, stress, circadian variations in insulin sensitivity, the
effect of counterregulatory hormones, rapidly acting insulin preparations (like Lispro), or endogenous insulin production (to simulate type 2 diabetic patients). Clearly such enhancements could add to the overall scope of the simulations. Similarly, occasionally missed insulin dosages, more sophisticated representations of meals, and random variations in BG concentrations could all add to the clinical realism of the simulations. Nevertheless, as shown in the AIDA case study above, a wide range of clinical scenarios can be simulated with the existing AIDA model.

Obviously the program will not be appropriate for all people. In particular such a program cannot be all things to all users. The wide range of experience and feedback obtained from the Web has demonstrated this very clearly. For example, some patients hope to be able to match AIDA’s simulations to their exact regimen and are disappointed if AIDA’s BG predictions do not exactly mirror what happens to their BG profile. As made clear in all the caveats that come with the AIDA software this is not the intended purpose of the educational simulator. In this respect, in 1994 an assessment was undertaken of the predictive accuracy of the AIDA model. Comparison of observed and predicted BG data from 24 type 1 diabetic patients over a period of 5–6 days revealed a mean (± SD) root mean square deviation between measured and simulated BG values of 34.7 ± 15.5 mg/dL (1.93 ± 0.86 mmol/L). While these ranges are too wide for clinical therapeutic use, for educational/demonstration/self-learning purposes predictive accuracy is not that important and values such as these should be sufficient.

Glycemic control is rarely the same for all people with diabetes because of a host of confounding variables. Not all these variables can be represented in a model such as AIDA. Furthermore, accurately parameterizing such models for individual patients remains problematic. For these reasons it needs to be stressed that the purpose of AIDA is to create a learning environment for communicating and training intuitive thinking when dealing with insulin dosage, dietary and lifestyle adjustments. The software is not meant for individual patient glycemic prediction or therapy planning. Also such a simulation program in no manner or form aims to compete with normal diabetes education. Rather it should be considered as a useful adjunct that may find a role in enhancing existing, standard education sessions. Given this, it needs to be recognized that the management of error is a key component of many learning processes. Identifying the error, getting patients or their relatives to discover it for themselves, and asking how they would correct it, are essential steps in educating patients how to improve their glycemic control. This author regards such processes as being very amenable to computer-based educational simulations. Experimenting with an interactive “virtual diabetic patient” may provide one harmless way for patients or their relatives to gain such experience.

In parallel with use for patient education, interactive diabetes simulators, like AIDA, may also have potential for the teaching of health care (medical/nursing) students, as well as other health care professionals about insulin dosage, dietary and lifestyle adjustments in diabetes mellitus. It is not difficult to envisage that a series of examinations and test cases could be integrated with AIDA and other computer-based learning tools to provide a complete computer-based lesson. However, in this era of evidence based medicine, evaluation studies will be needed first to establish the general efficacy of the computer-assisted learning/interactive simulation approach.

SYSTEM AVAILABILITY

The AIDA software can be obtained without charge from the Diabetes UK Internet site at http://www.diabetic.org.uk/aida.htm on the World Wide Web. The program runs under DOS/Windows on IBM PC or compatible 80386/486/Pentium-based machines and requires approximately 3 Mb of hard disk storage space. AIDA can also be used on Apple Macintosh computers running SoftWindows v2.0 or later.

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**REFERENCES**


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