

surgical side down and decreasing mean airway pressure. Injecting air into the surgical hemithorax may also be helpful. The return of normal vital signs allows a safer return to the operating room and surgical closure of the pericardium. If conservative measures fail to produce hemodynamic stability, immediate thoracotomy and reduction of the heart and great vessels are indicated.

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A Comparison of Two Regimens for the Management of Diabetes during Open-heart Surgery

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Recent evidence suggests that operative mortality may be higher in diabetics than in non-diabetics undergoing coronary artery bypass grafting.^{1,2} Morbidity may also be higher in diabetics undergoing coronary artery bypass grafting, as indicated by significantly increased frequency

of inotropic therapy and intra-aortic balloon pump support during the postoperative phase.³

The reasons for this increased morbidity and mortality are not clear, although it is possible that poor perioperative metabolic control may be contributory. The metabolic consequences of open-heart surgery with cardiopulmonary bypass predispose to difficulties in control of diabetes mellitus during that surgery.⁴ Of particular importance are the marked hyperglycemia and insulin resistance associated with cardiopulmonary bypass, associated themselves with increases in blood levels of catecholamines, cortisol, vasopressin, and growth hormone in the absence of any increase in serum insulin concentration.^{3,††}

Kuntschen *et al.*⁵ recently reported good blood glucose and intermediary metabolite control in diabetic patients undergoing coronary artery bypass grafting utilizing

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Biostator^{‡‡} feedback control of blood glucose. In this report we compare the use of Biostator control of blood glucose during open-heart surgery with a simpler, open-loop method of management.

METHODS

Twelve consecutive known diabetic patients presenting for open-heart surgery over a six-month period were studied.^{§§} All patients were admitted at least three days prior to surgery and informed consent obtained from each. Preoperative management of their diabetes up until the night before surgery was as recommended by Alberti et al.⁶ Patients were allocated randomly to receive one of two management regimens during surgery. One group of patients (group A, $n = 7$) was assigned to closed-loop, Biostator feedback blood glucose control. The second group of patients (group B, $n = 5$) was to receive open-loop control of blood glucose by variation of insulin infused via syringe pump on the basis of frequent blood glucose estimations (using Dextrostix; Ames, Elkhart, Indiana, and the Glucometer; Ames).

When satisfactory blood glucose control was achieved the night before surgery, a peripheral intravenous infusion of glucose, 10% in water was commenced in each patient at a rate of $1 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ ($0.1 \text{ g glucose} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$). The patients in group A also were connected to the Biostator with constants set to maintain blood glucose between 5 and 6 mmol/l.^{¶¶} The patients in group B were each connected to a syringe pump insulin infusion [1 ml of 40 U/ml Actrapid (Novo) insulin in 39 ml of Haemacel; 1 ml of infusion = 1 U insulin], and hourly blood glucose estimations were performed on samples taken from an indwelling venous cannula using Dextrostix and Glucometer reading. Insulin infusion rate was adjusted by one of the authors to maintain the blood glucose level as close as possible to 7 mmol/l. Insulin requirements were recorded.

On transfer to the operating theater the following morning (approximately 0745 h), the glucose infusion was stopped in both groups. The insulin infusion in group B was continued at 0.3 U/h as a basal infusion. Biostator feedback control was continued in group A. In theater no glucose or lactate containing fluids were infused in either group, as recommended by Thomas and Alberti.⁷ Crystalloid fluid requirements were met by Plasmalyte 148 (Travenol Ltd.) and the same solution was used to prime the cardiopulmonary bypass circuit. [Whole blood

TABLE 1. Blood Sampling Regimen and Sample Numbers

Sampling Regimen
1. 0500 h on day of operation
2. 0600 h on day of operation
3. 0700 h on day of operation
4. 5 min after induction of anesthesia
5. 5 min after skin incision
6. 5 min after heparinization
7. 5 min after onset of cardiopulmonary bypass
8. 15 min after onset of cardiopulmonary bypass
9. 30 min after onset of cardiopulmonary bypass
10. 60 min after onset of cardiopulmonary bypass
11. 5 min before the end of cardiopulmonary bypass
12. 5 min after protamine injection
13. 1 h postoperatively
14. 2 h postoperatively
15. 4 h postoperatively

(acid-citrate-dextrose) was added to the prime in three cases because of preoperative anemia]. All solutions for flushing intravascular pressure lines were of normal saline (0.15 M).

In group A, feedback control of blood glucose using the Biostator continued throughout surgery. In group B, blood glucose estimations (Dextrostix read by Glucometer) were performed every five minutes during the operation, and the insulin infusion rate adjusted to maintain blood glucose as close to 7 mmol/l as possible.

On completion of the operation, each patient was transferred to the adjacent intensive care unit, where a 10% glucose in water infusion was initiated at $1 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. In group A, feedback control of blood glucose continued until at least 4 h postoperative and until a stable insulin requirement was observed. In group B, blood glucose sampling was reduced to every 15 min postoperatively and, after 4 h, to hourly samples. Insulin infusion was adjusted as described above.

In addition to the above sampling, frequent metabolic profiles (glucose, lactate, pyruvate, alanine, glycerol, and 3-hydroxybutyrate) were obtained from all patients, at the times shown in table 1. Metabolite estimations were carried out by an automated fluorometric assay.⁸ Statistical analyses were performed using Students' *t*-tests, paired within groups and unpaired between groups.

RESULTS

Clinical details of the patients studied are shown in table 2. Operative details are shown in table 3.

Two patients in group A and one in group B underwent cardiopulmonary bypass at normothermia. All other procedures were carried out at 28°C, the differentiation being entirely dependent on the preference of the various surgeons.

It can be seen from figure 2 that blood glucose was maintained <7 mmol/l in both groups preoperatively.

^{‡‡} BIOSTATOR glucose controlled insulin infusion system, Miles Laboratories Ltd., Elkhart, Indiana.

^{§§} The protocol has been approved by the Area Ethical Committee.

^{¶¶} In practice we have found that with constants so set blood glucose settles out at around 7 mmol/l. (To convert mmol/l to mg/dl, multiply by 18).

TABLE 2. Details of Patients Studied

	Group A (Closed-loop)	Group B (Open-loop)
n	7	5
Age (yr)	57 ± 2	48 ± 9
Sex	4F, 3M	2F, 3M
Height (m)	1.63 ± 0.02	1.66 ± 0.02
Weight (kg)	71 ± 2	60 ± 6
Diabetes*		
Type I	2 patients	2 patients
Type II	5 patients	3 patients
Insulin-dependent	4 patients	3 patients

* Type I = juvenile onset; Type II = maturity onset.

Blood glucose concentrations in group A (closed-loop) were greater than those in group B (open-loop) during this phase. This probably represents a characteristic of the Biostator control in these patients, since in none of them was the blood glucose as low as the pre-programmed value of 6 mmol/l.

After skin incision and before cardiopulmonary bypass, blood glucose concentrations were maintained <8 mmol/l (in both groups), but on bypass were observed gradually to increase. Blood glucose remained slightly increased throughout cardiopulmonary bypass in both groups, and re-warming was associated with a more rapid increase. After cardiopulmonary bypass and before the end of surgery, blood glucose remained moderately increased in both groups. Blood glucose was maintained at less than 10 mmol/l throughout surgery.

Following transfer to the intensive care unit, blood glucose remained elevated in group A. Problems were encountered in obtaining continuous sampling for the

TABLE 3. Details of the Operations Performed

Operations	Closed Loop Group A	Open Loop Group B
MVR and CABG	2	1
CABG	2	1
MVR	1	3
TVR	1	
AVR	1	
Operative duration (min)	261 ± 11	274 ± 20
Bypass duration (min)	106 ± 11	123 ± 12
Aortic cross clamp time (min)	54 ± 10	64 ± 6
Bypass temperature 37° C	2 patients	1 patient
28° C	5 patients	4 patients

MVR = mitral valve replacement; AVR = aortic valve replacement; TVR = tricuspid valve replacement; and CABG = coronary artery bypass grafts.

Biostator in several of the group A patients. In three, difficulties caused by peripheral vasoconstriction, movement of the patient, and nursing procedures resulted in more prolonged interruptions in sampling. This resulted in the Biostator delivering submaximal insulin doses during the interruptions in feedback, and blood glucose values increased. In group B, values for blood glucose had decreased to 5.8 ± 0.7 mmol/l by four hours postoperatively.

Insulin requirements during the various phases of the procedure are shown in table 4. There was no significant difference in insulin requirements between groups at any stage, other than the period from skin incision to the onset of cardiopulmonary bypass. During this phase, > 0.3

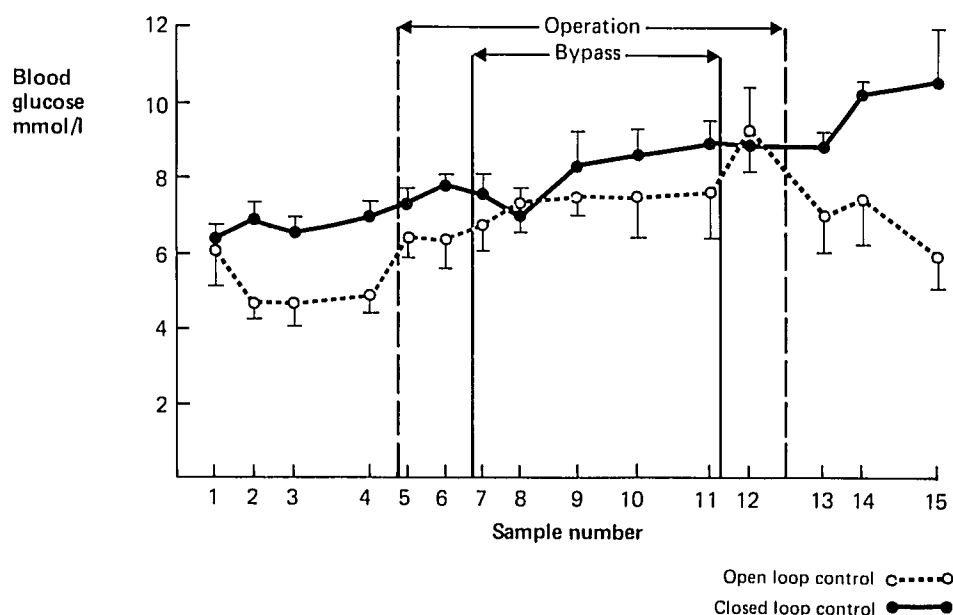
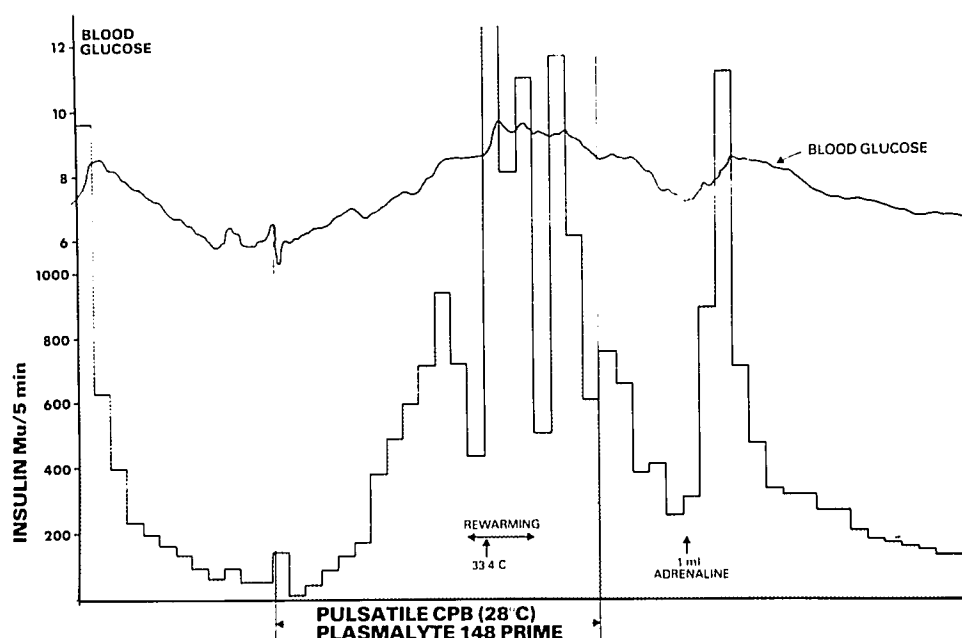


FIG. 1. Blood glucose results (mmol/l). Sample numbers are explained in table 1.

FIG. 2. Biostator record of the control of an insulin-dependent diabetic undergoing coronary artery bypass grafting. The figure covers the operative period. Blood glucose (mmol/l) is shown as the continuous line, and insulin delivery (mU/5 min) as the histogrammic bars. For discussion, see text.



U/h insulin was infused in group B patients only if Dextrostix showed a blood glucose > 7 mmol/l, whereas in group A, feedback control assured continuous insulin infusion. Insulin requirements increased in both groups during bypass, and to approximately sevenfold greater than preoperative requirements during the first four hours postoperatively, despite the same rate of glucose infusion.

No significant differences were noted between groups at any stage, in blood levels of lactate, pyruvate, alanine, 3-hydroxybutyrate, and glycerol.

Certain important and consistent changes were exposed by the continuous monitoring obtained by the Biostator. An example of such a record is shown in figure 2. Specific phases of the procedure were associated with increased insulin delivery. These phases were cardiopulmonary bypass, rewarming at the end of hypothermic cardiopulmonary bypass, and after the injection of 1 ml of 1/10,000 adrenaline into the aortic root. Insulin delivery increased to >20 U/h during rewarming and after the injection of adrenaline. Similar changes were observed in all the group A patients, and in some of them, increased insulin delivery was noted in association with post-bypass ACD (acid-citrate-dextrose) blood transfusion. In group B patients, insulin requirements were observed to increase at similar stages of the procedure.

DISCUSSION

Blood glucose control during open-heart surgery can be achieved by Biostator feedback because of the rapidity of response of that system.⁵ However, a Biostator is not

always available in cardiothoracic units, and even if one is available, certain practical difficulties exist in its application. It is a complex, labor-intensive, and large machine which has the additional disadvantages of being reliant on a double-lumen peripheral-venous sampling line to provide the continuous blood sample required for analysis. This is a disadvantage in the context of open-heart surgery since the associated hemodynamic and temperature variations can result in intense peripheral vasoconstriction with resultant interruption in sampling and thus feedback regulation.

We demonstrated in this study that an appropriately managed open-loop technique can provide at least as good blood glucose control as the established Biostator technique. The sampling problems encountered in group A suggest that the simple, open-loop system actually may be superior, particularly in the postoperative phase. Insulin requirements were observed to be similar in both

TABLE 4. Insulin Requirements of the Two Study Groups During Various Phases of the Perioperative Period

	Insulin Requirements (units/h; mean \pm SEM)	
	Closed Loop	Open Loop
Preoperatively	1.6 \pm 0.2	1.4 \pm 0.3
Skin incision to onset of bypass	3.0 \pm 1.0	0.5 \pm 0.2
During bypass	5.0 \pm 1.2	3.6 \pm 1.6
First half hour after bypass	8.3 \pm 0.9	8.9 \pm 2.4
First four hours postoperatively	12.3 \pm 2.6	9.0 \pm 3.7
Total insulin infused during surgery (u)	21 \pm 2.4	21.4 \pm 9.3

groups, and no significant differences were noted in intermediary metabolite concentrations. The values for glucose and intermediary metabolites were within the ranges observed for non-diabetic patients undergoing open-heart surgery with similar techniques in our unit (unpublished data). This study also demonstrated the safety of using insulin without added glucose in the procedure, in contrast to our usual practice.⁶

Analysis of the Biostator records of the group A patients confirmed the insulin resistance said to be associated with cardiopulmonary bypass. Such analysis also revealed certain other features of importance for the management of diabetes. First, in all patients undergoing hypothermic cardiopulmonary bypass, rewarming was associated with a rapid increase in blood glucose (range 1–3 mmol) and a concomitant increase in insulin requirements. In non-diabetic patients on continuous blood glucose monitoring the blood glucose decreases rapidly after this initial increase with rewarming, in association with the return of insulin secretion with normothermia. Catecholamine levels are known to be increased during hypothermic cardiopulmonary bypass,^{8,9} and likely stimulate hepatic glucose production; furthermore, the activity of the enzyme systems involved is increased at perfusion temperatures >33°C.

Second, blood glucose concentration and insulin requirements increased rapidly in those patients who required post-bypass transfusion of acid-citrate-dextrose stored blood with its attendant glucose load, estimated at 10–20 mmol/l, and a lactate load of 6–10 mmol/l.

Third, blood glucose concentration and insulin requirements increased rapidly after the infusion of inotropic agents, particularly adrenaline, in those patients who required them. Thus, rewarming, transfusion, and inotrope therapy represent phases of the procedure when rapid changes in blood glucose and in insulin requirement are to be expected. The frequency with which blood glucose estimations were performed in group B (every five minutes) was adequate to provide the rapid response in insulin infusion rate necessary to maintain blood glucose

control. It is likely that the frequency of sampling in between these phases could be reduced. Further work is in progress to determine the optimum sampling regimen.

We conclude that diabetic patients, both insulin-dependent and non-insulin-dependent, requiring open-heart surgery with cardiopulmonary bypass can be adequately controlled metabolically with either closed-loop (Biostator), or open-loop (frequent blood glucose estimations and insulin via syringe pump) methods. Preoperative stability is mandatory and committed care is essential during and after surgery. It is not known whether the improved perioperative metabolic control of diabetes will improve prognosis, but at least one major potential contributor to morbidity is neutralized.

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