Olympic diabetes

What have we learned over the last decade?

PROFESSIONAL ISSUES

Olympic diabetes

Ian W Gallen, Ann Redgrave and Steven Redgrave

ABSTRACT – Winning an Olympic gold medal represents the pinnacle of achievement in any sporting event, to do so with diabetes is almost miraculous. This report outlines the history and management of Steven Redgrave's diabetes, and describes the physiology associated with the extremes of human endurance and the difficulties that this presents.

KEY WORDS: diabetes type 1, diabetes type 2, exercise, exercise physiology, glucose metabolism, glucose storage, insulin lispro, rowing

Case report

Steven Redgrave, then 35 years old, presented in September 1997 with a classical history of diabetes: a short history of insatiable thirst, marked polyuria, a weight loss (ca 2–3 kg) and a marked loss of athletic performance. His general practitioner promptly diagnosed diabetes and referred him to the Chiltern Diabetes Centre. He was an internationally competi-

Analysis suggested excessive Isophane insulin action. Evening Isophane insulin was reduced, but daytime analogue injections were increased. The insulin regimen at this time is shown in Table 1. His blood sugar control during this period was excellent (4–10 mmol throughout the day). His glycosylated haemoglobin was 7.4%.

Over the next year his diabetes was managed with 6–8 units of Lispro insulin four times a day. There was a steady improvement in his athletic performance, with his crew winning the 1998 World Rowing Championships. As usually happens following initiation of insulin therapy, the dose had to be increased substantially. During winter training in 1999, Steven again noticed marked loss of performance after 2–3 minutes of exercise, with a rapid heart rate. No obvious cause for his loss of stamina was found. Other hormonal disorders and an exacerbation of his colitis were excluded.

A review with his coach, physiologist, dietitian and physician concluded that the carbohydrate intake was probably insufficient to support the level of

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Sir Steven Redgrave CBE DSc(Hon), Olympic Gold Medallist

Clin Med 2003;3:333–7

Ian Gallen

Jephcott Symposium

9th May 2012

The Royal Society of Medicine

Diabetes and exercise

Ian Gallen

Challenges in the management SR's diabetes prior to 2000 Olympic games

- How to give insulin treatment with high enough energy intake
- How to give basal insulin and avoid hypoglycaemia during exercise
- How to avoid nocturnal hypoglycaemia
- Identify and treat excessive fatigue
- Restore pre-existing performance

What did we need to know?

Effect of exercise on blood glucose	
Differences between types of exercise	
Timing, type and quantity of carbohydrate	
What to do with bolus insulin dose	
What to do with basal insulin dose	
Nocturnal hypoglycaemia	
Causes and treatment of fatigue	
How to use insulin pump treatment	

What do we need to know

Effect of exercise on blood glucose

Differences between types of exercise

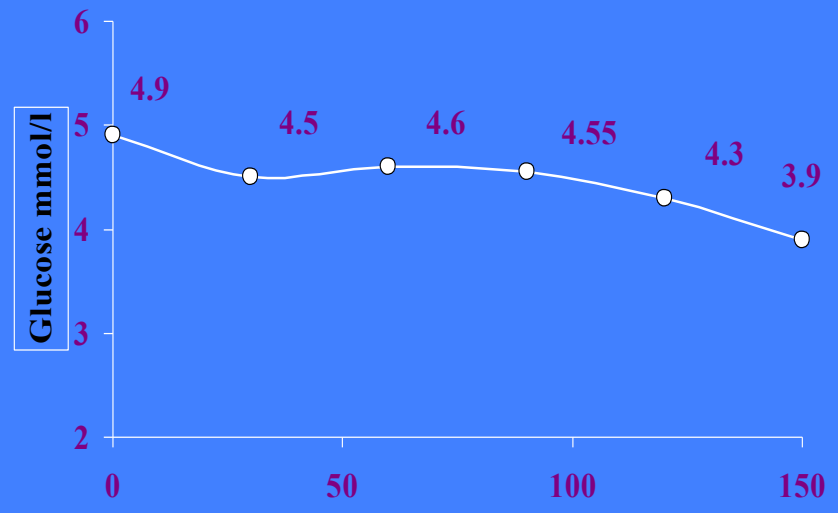
Timing, type and quantity of carbohydrate

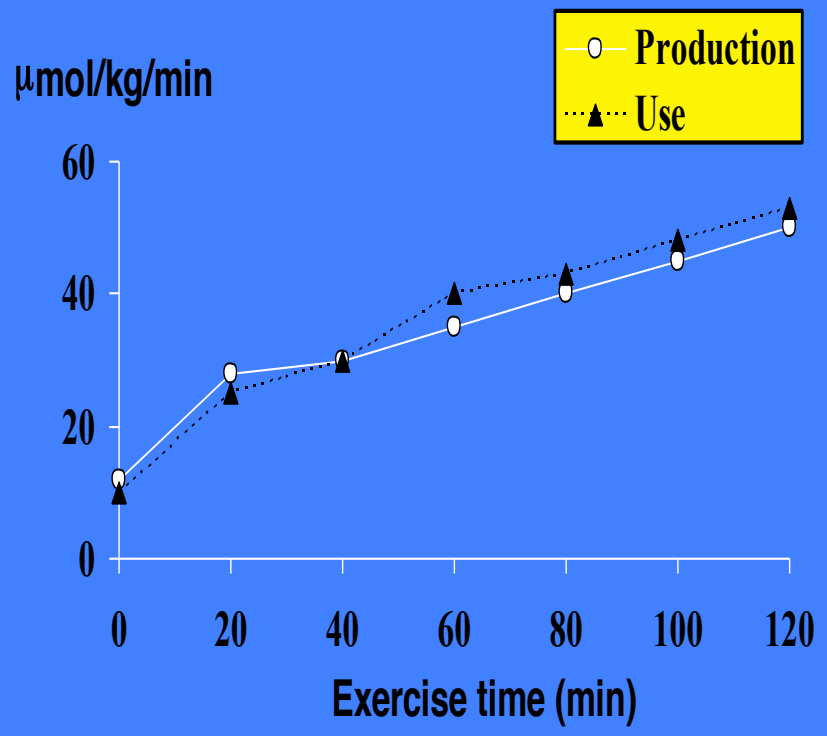
What to do with insulin dose

Nocturnal hypoglycaemia

How to use insulin pump treatment

Glucose metabolism during exercise





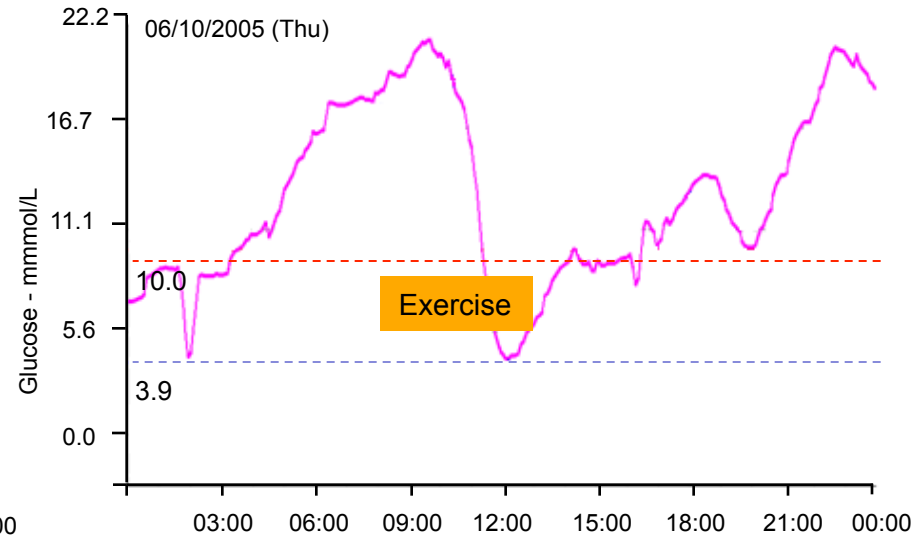
McConell et al. 1994

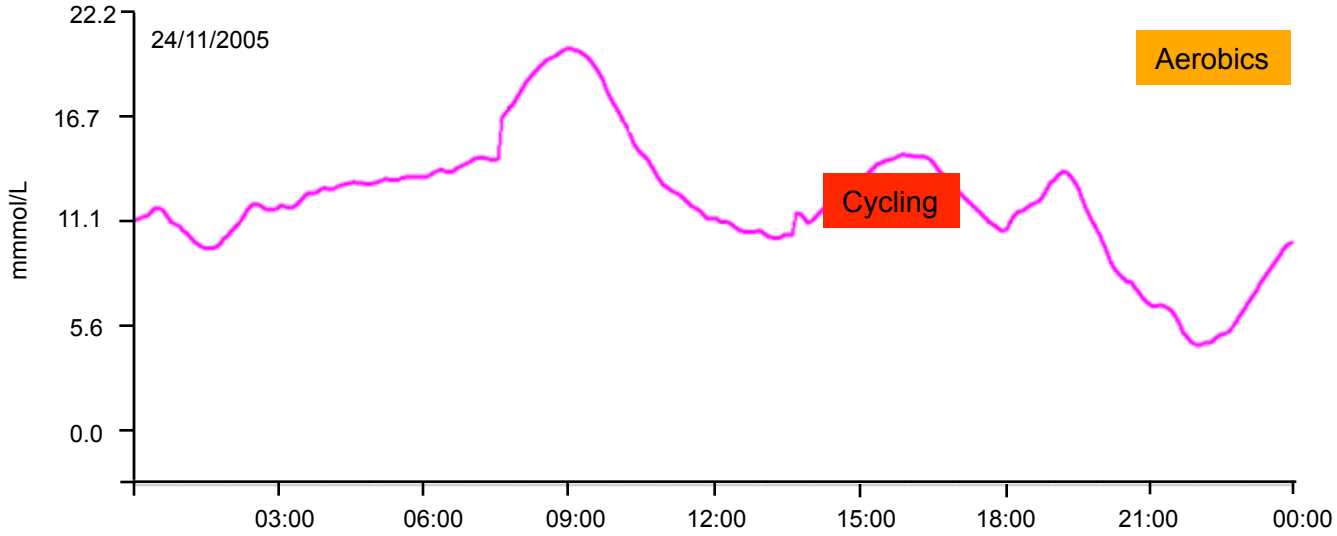
What is different about exercise in diabetes?

- Food storage
  - Athletes require high energy intake of high glycaemic index foods.
- Usually excessive background insulin levels
- Endocrinology of exercise
  - Abnormal glucagon response
  - Abnormal portal insulin regulation of gluconeogenesis and ketogenesis
  - Impaired catecholamine response

- Diabetic complications
  - Autonomic neuropathy/microvascular disease

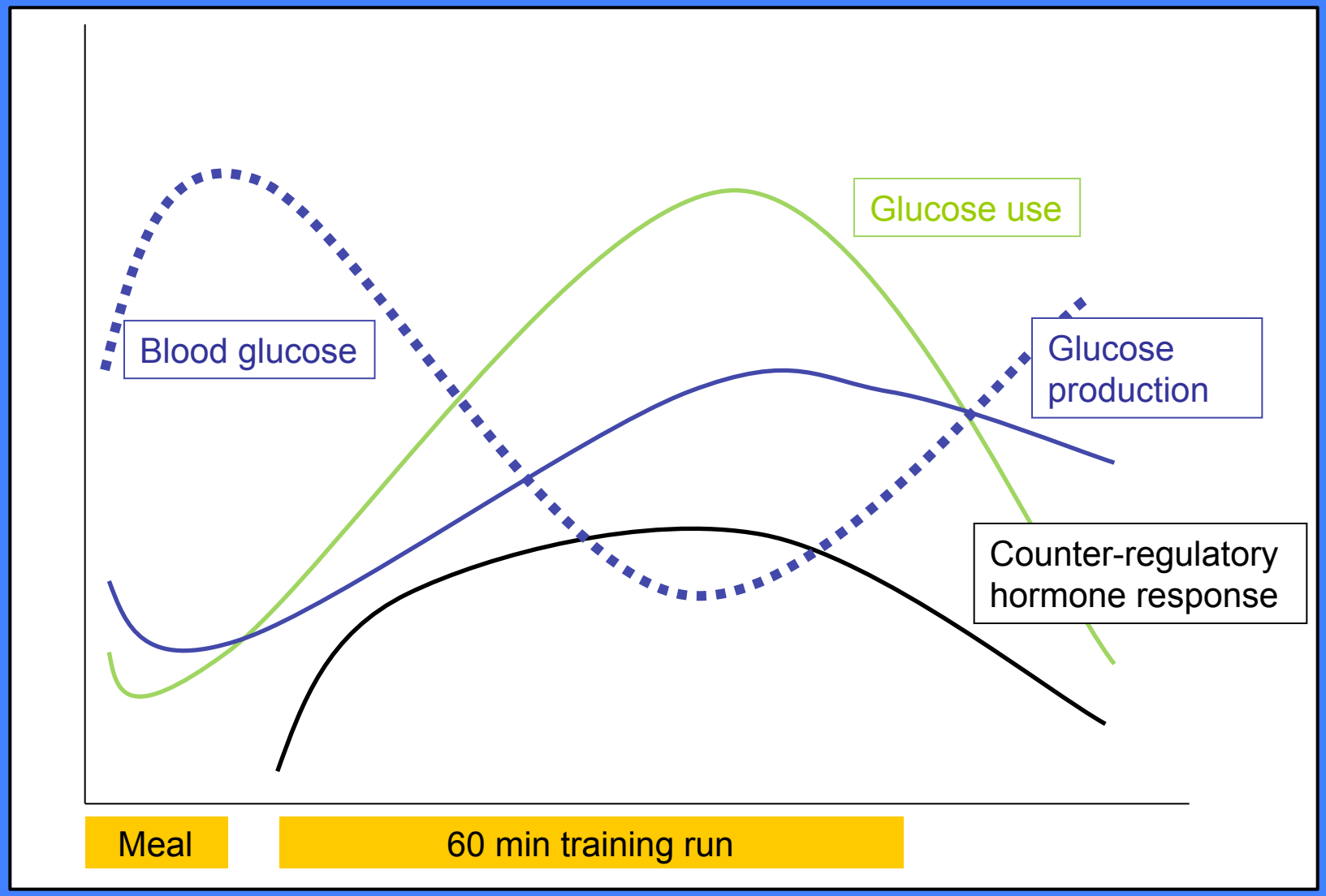
What Happens to Blood Glucose in Exercise in Type 1 Diabetes?



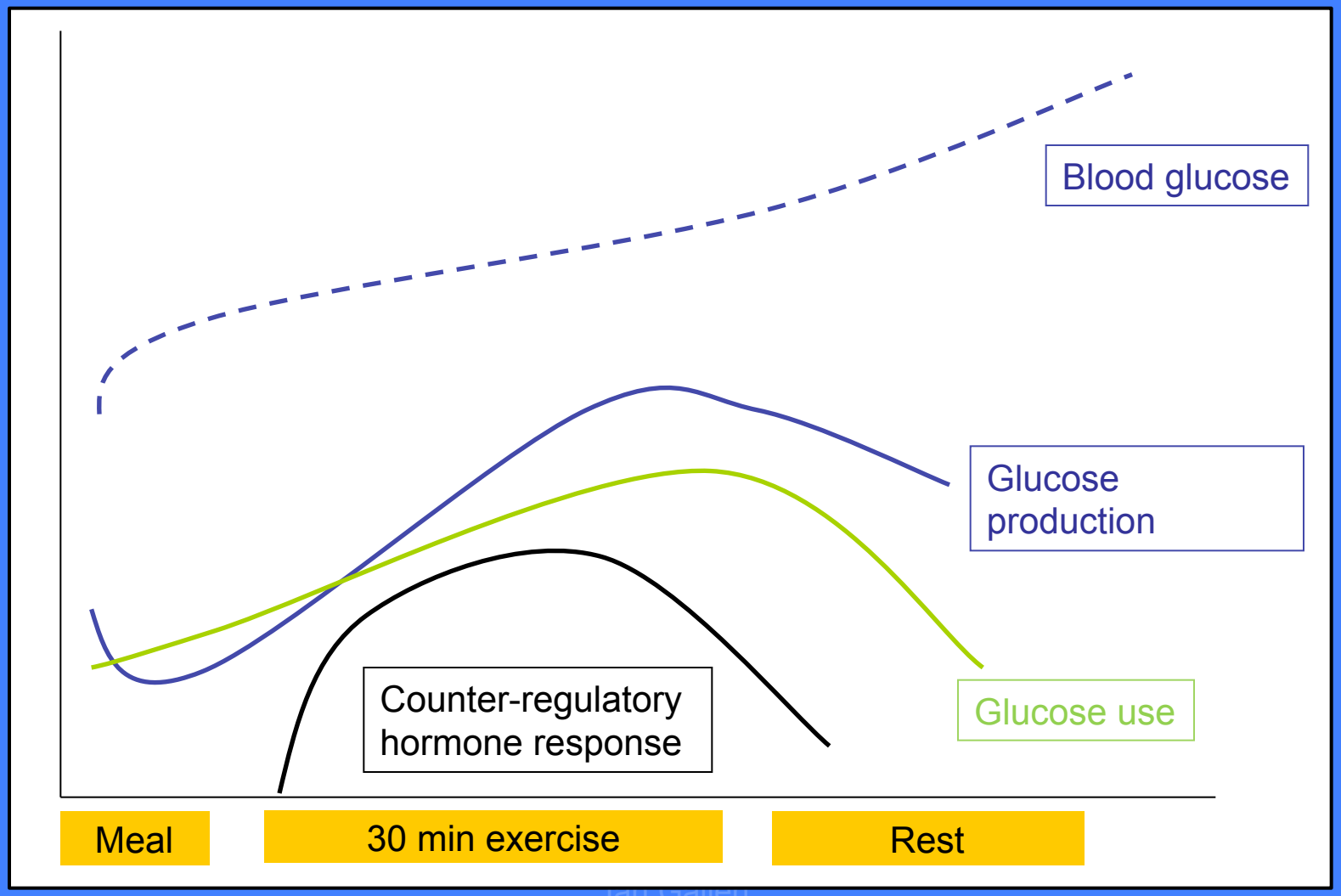


Data from Buckinghamshire Hospitals Diabetes Sports clinic

Trends in Glucose Production and Use in T1DM During Prolonged Aerobic Exercise



Trends in Glucose Production and Use in T1DM During Short Intense Exercise



Effect of high or low intensity exercise on blood glucose in T1DM

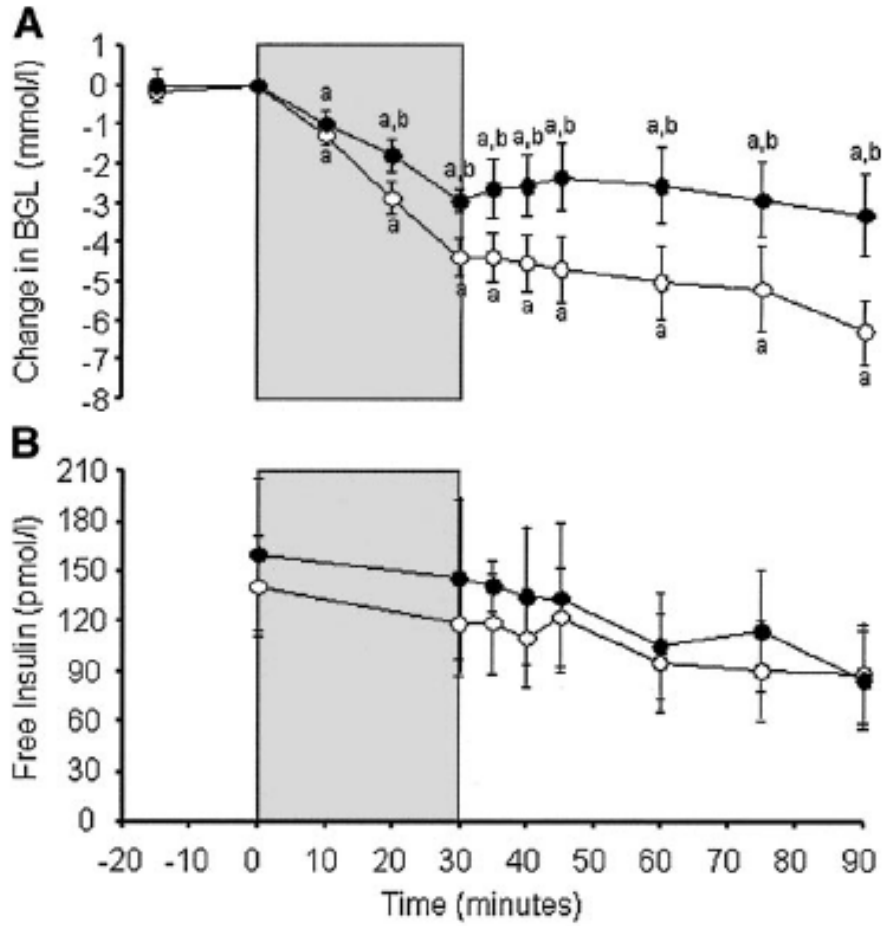


Figure 1—*Effect of 30 min (represented by box) of IHE (■) or MOD (□) on normalized blood glucose levels (A) and free insulin levels (B). Results are expressed as means ± SE.* [a]*Statistically significant difference (P < 0.05) from resting.* [b]*Statistically significant difference (P < 0.05) between IHE and MOD.*

DIABETES CARE, VOLUME 28, NUMBER 6, JUNE 2005

Blood glucose and metabolite response during exercise in T1DM

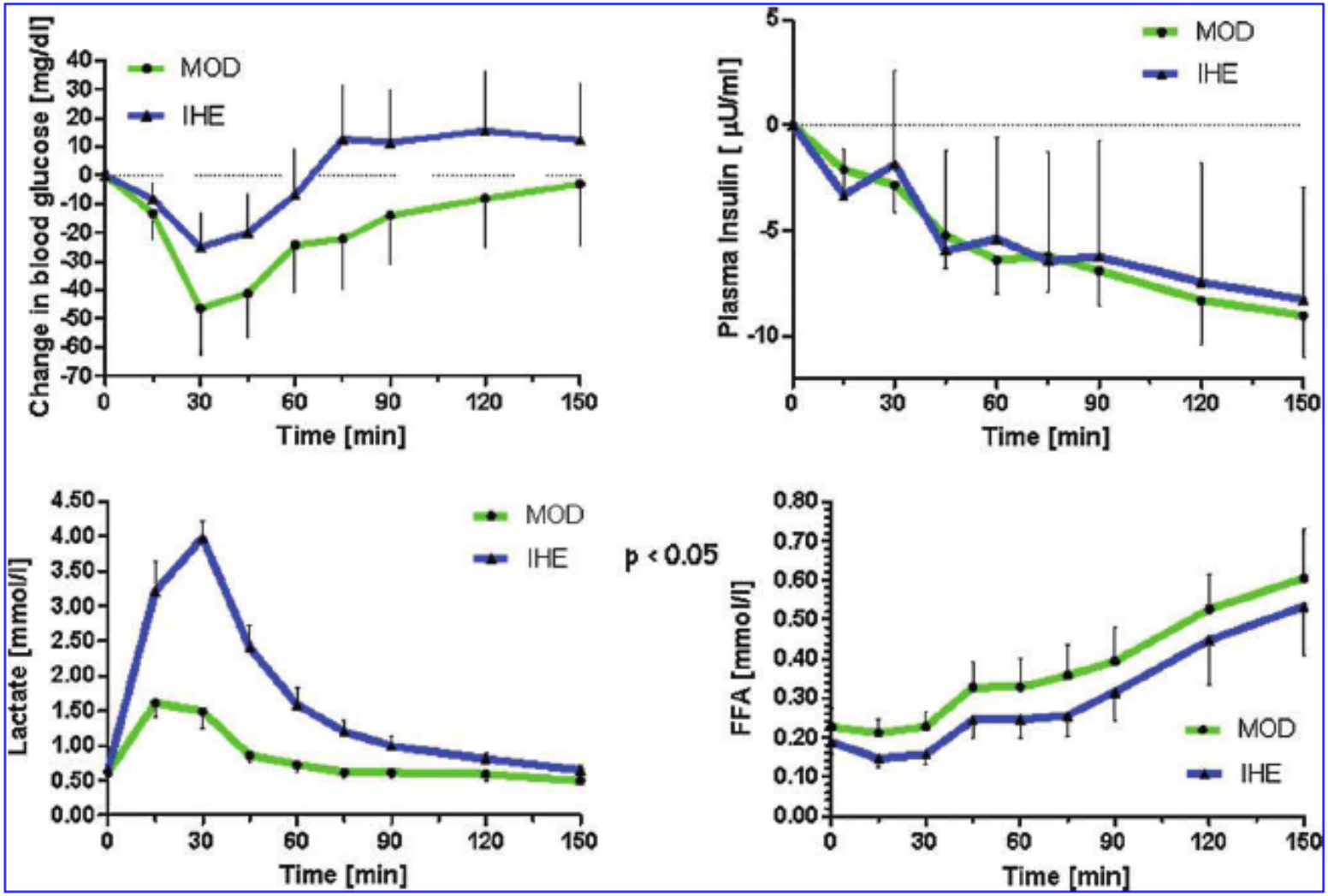


FIG. 2. Changes in blood glucose (**upper left panel**), plasma insulin (**upper right panel**), blood lactate (**lower left panel**), and plasma free fatty acids (FFA) (**lower right panel**) during moderate-intensity exercise (MOD) (green lines) and during intermittent high-intensity exercise (IHE) (blue lines). Data are mean ± SEM values. Color images available online at www.liebertonline/dia.

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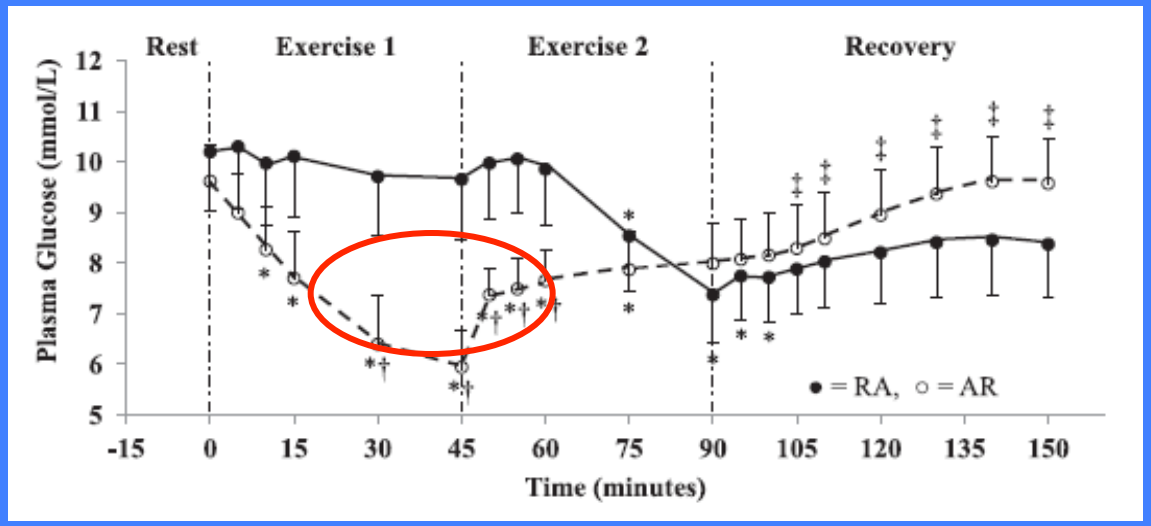
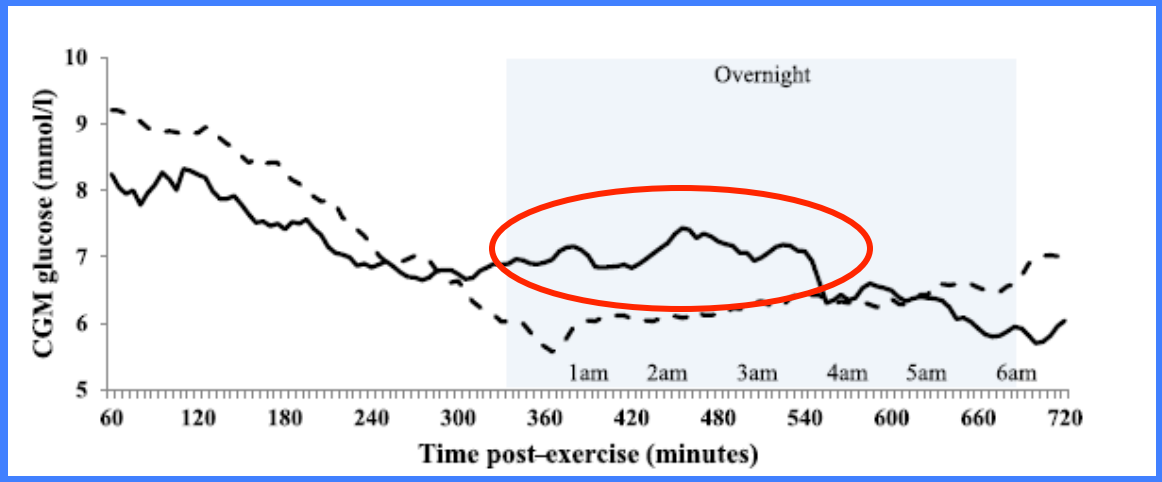
Glucose levels during and following different forms of exercise



Aerobic first

Resistance first



Aerobic first

Resistance first

Diabetes Care 35:669–675, 2012

Hypoglycaemia is frequent following aerobic and resistance training

Table 2—*Summary of overnight (2400 to 0600 h) continuous glucose monitoring data for the night before and the night after exercise**

	AR (n = 12)	RA (n = 12)
Night before exercise session		
Participants experiencing nocturnal hypoglycemia†	4 (30)	5 (42)
Total hypoglycemic episodes	7	4
Duration of hypoglycemia per episode (min)	97.5 ± 84.9	47.1 ± 32.8
AUC for hypoglycemia per episode (mmol · min)	112.3 ± 97.6	42.3 ± 41.9
Overnight glucose (mmol/L)	6.7 ± 3.2	6.9 ± 2.7
Night after exercise session		
Participants experiencing nocturnal hypoglycemia†	3 (25)	4 (30)
Total hypoglycemic episodes	5	6
Duration of hypoglycemia per episode (min)	105 ± 116	48 ± 68
AUC for hypoglycemia per episode (mmol · min)	110 ± 146	59 ± 110
Mean overnight glucose (mmol/L)	6.3 ± 2.4	6.7 ± 3.1

Categoric data are expressed as n or n (%), and continuous data are presented as mean ± SD. *No significant differences between pre- and postexercise, or between exercise conditions. †Defined as glucose <3.5 mmol/L.

Diabetes Care 35:669–675, 2012

Effects of exercise on blood glucose

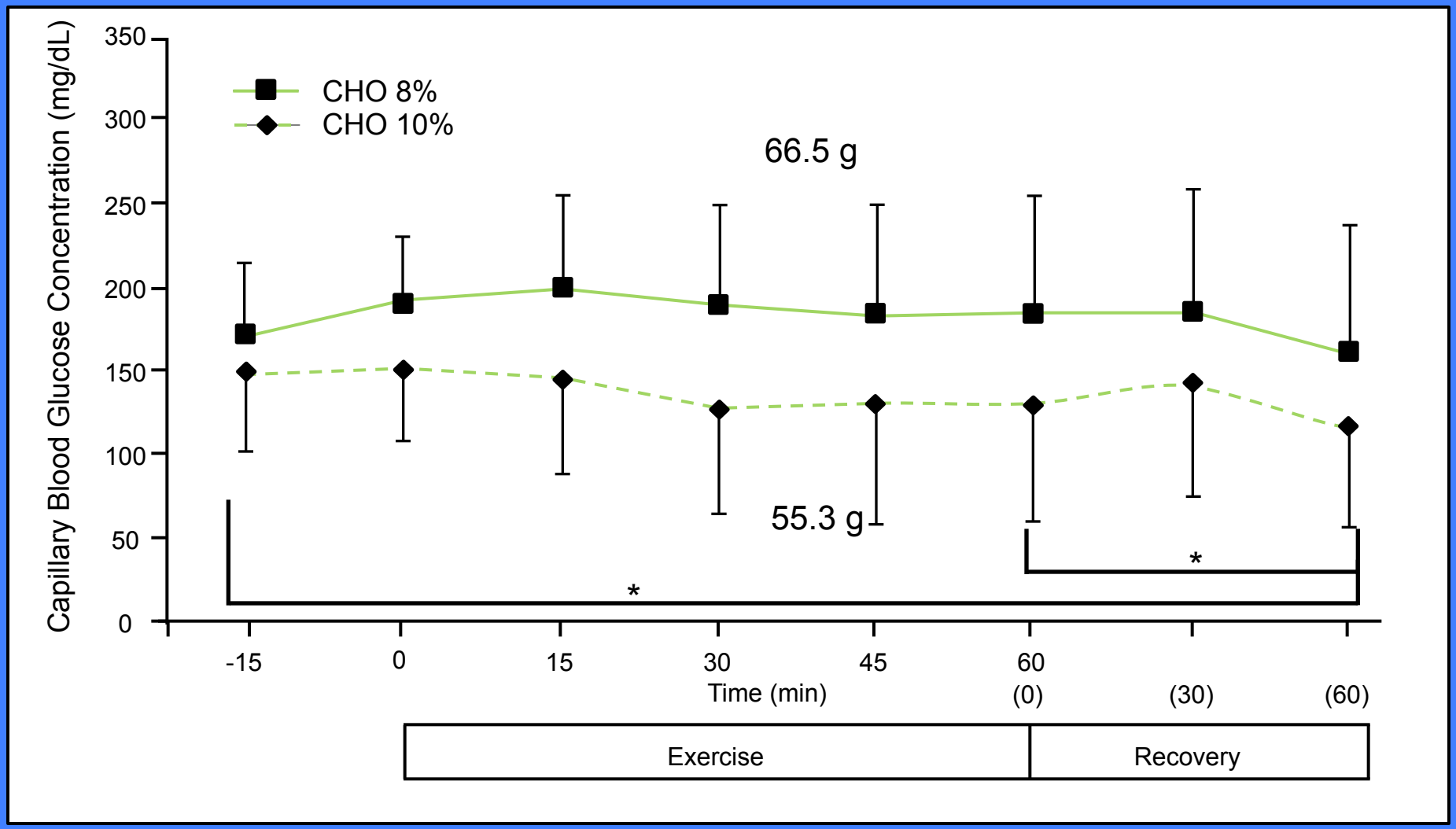
- Aerobic exercise causes blood glucose to fall rapidly
- Anaerobic exercise cause blood glucose to rise
- Aerobic exercise increases risk of nocturnal hypoglycaemia
- Intermittent high intensity exercise protects against hypoglycaemia during exercise, but is more likely to cause nocturnal hypoglycaemia
- Team sports have variable effect on glucose depending on position and intensity of play

Carbohydrate support

Why not just start with a high glucose? Some mathematics

- Available free glucose space is 20% lean person total weight
- 1mm/l measured glucose is 0.18g free glucose or total 2.5g in 70 kg person
- Thus raising bg to 15mmol/l, will only provide 25g readily available glucose.
- At 60%vO_2 max glucose oxidation typically 130 µmol/kg/min.
- Thus approximately 2g/min or 12 minutes!

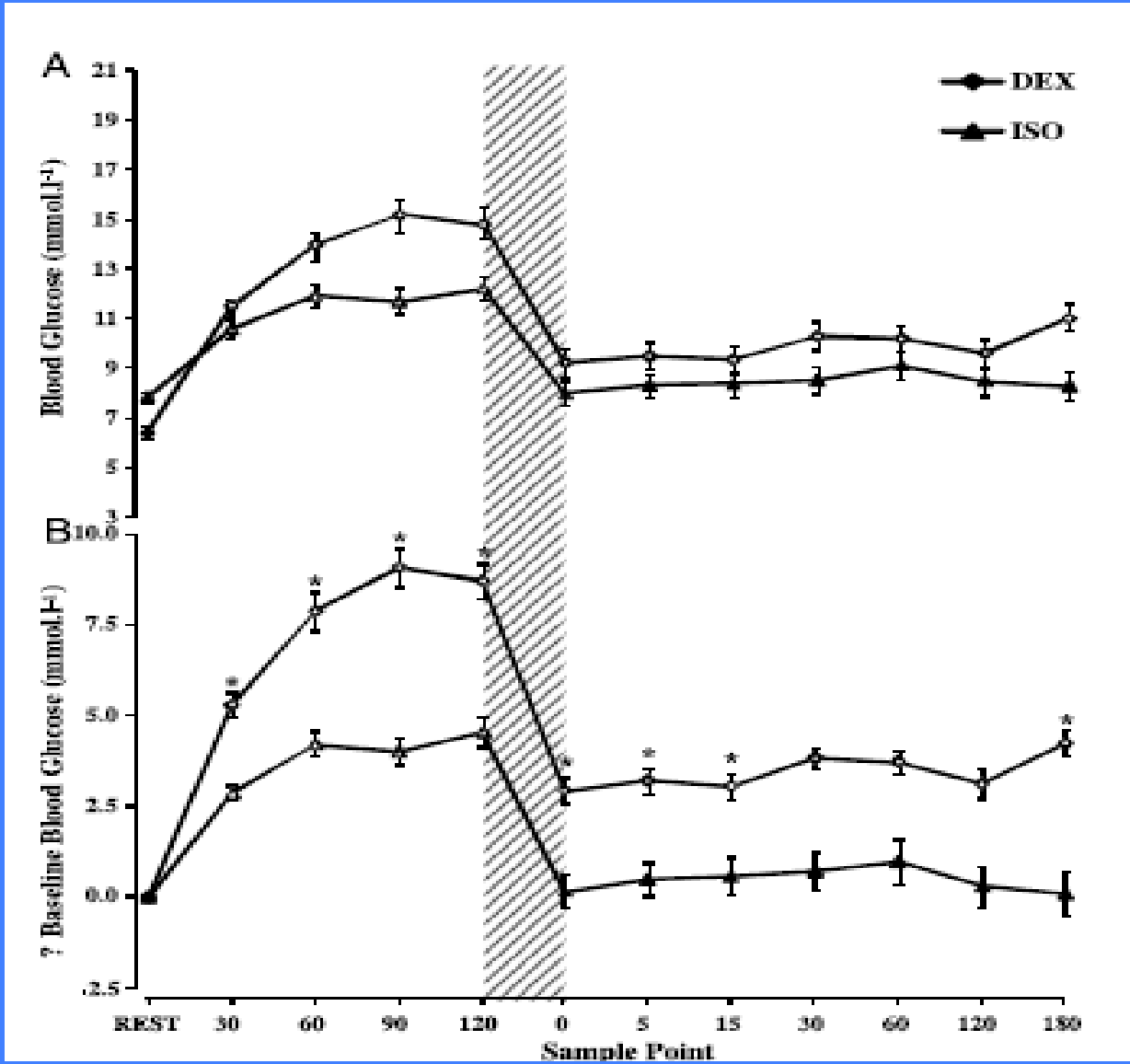
Effect of Carbohydrate Ingestion on the Glycaemic Response of Type 1 Diabetic Adolescents During Exercise



Data are means ± SD; *p<0.05.

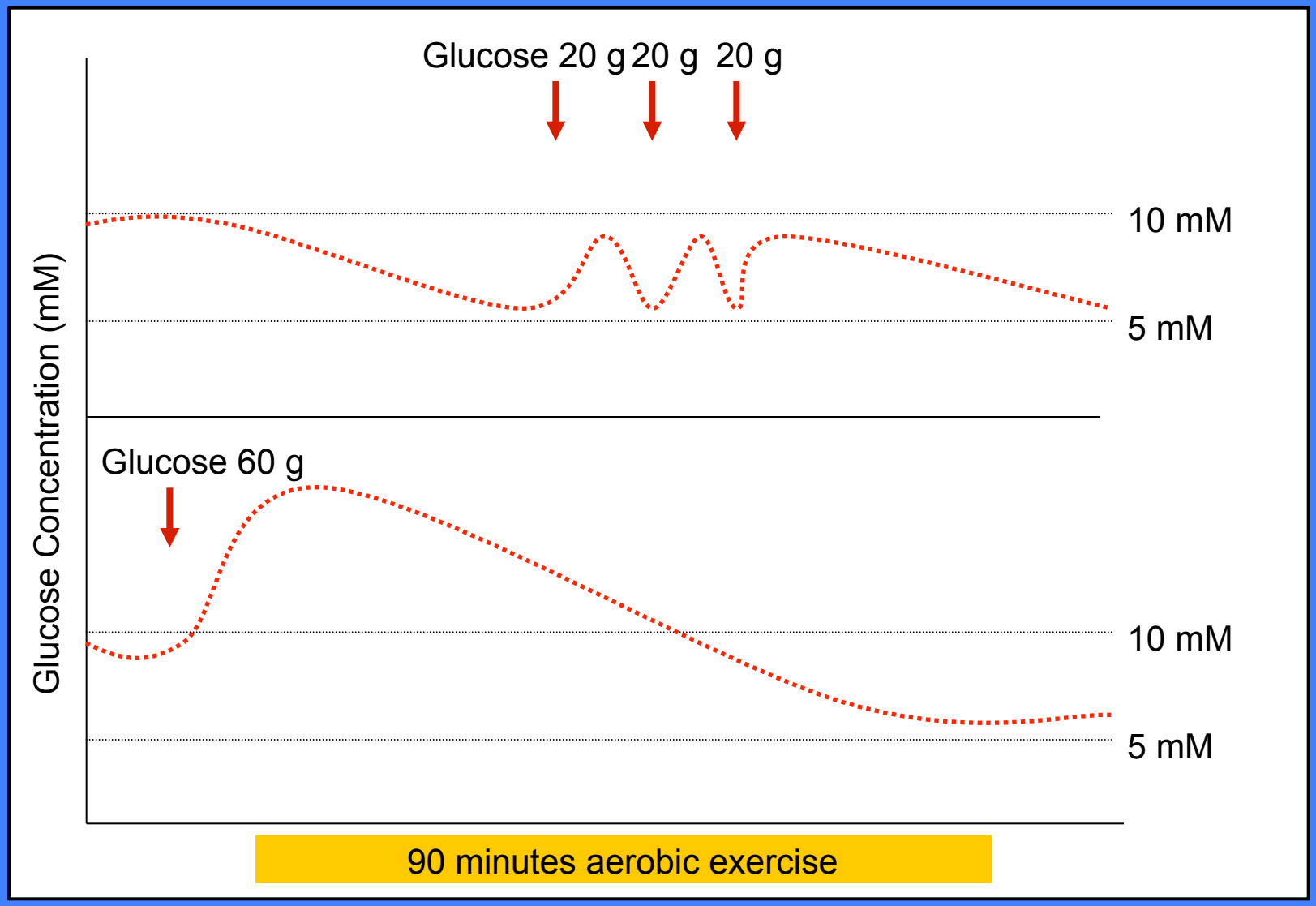
Perrone C, Laitano O, Meyer F. *Diabetes Care*. 2005;**28**:2537–2538.

75g Isomaltulose or dextrose before exercise in T1DM

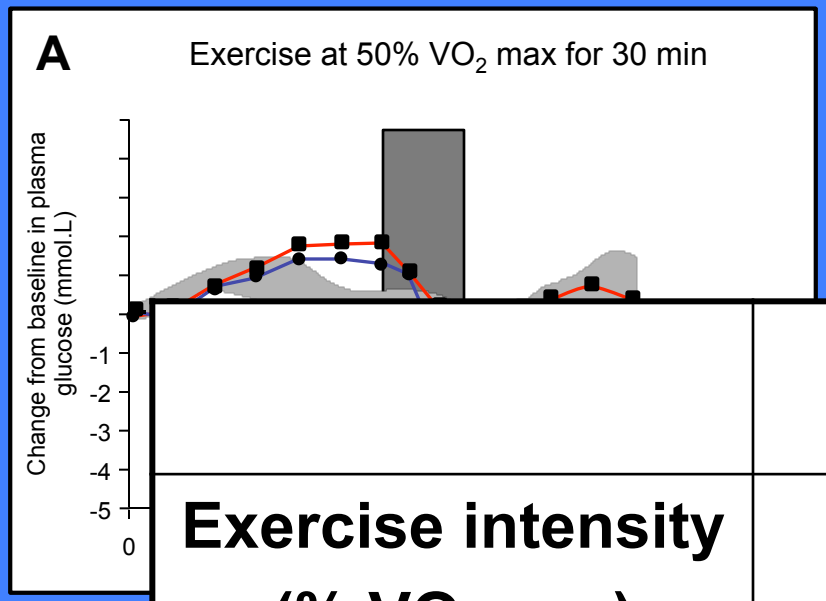


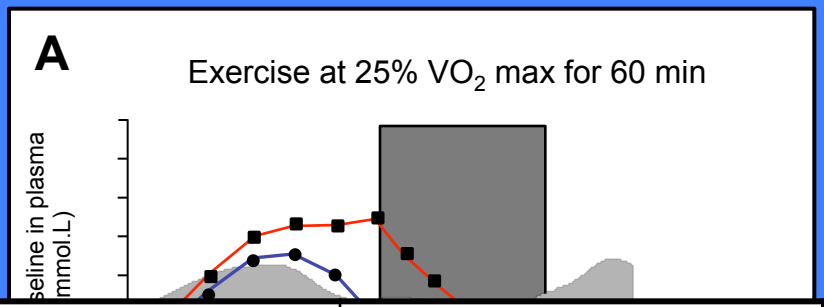
West et al, 2011 MEDICINE & SCIENCE IN SPORTS & EXERCISE®

Strategies for Glucose Replacement During Exercise

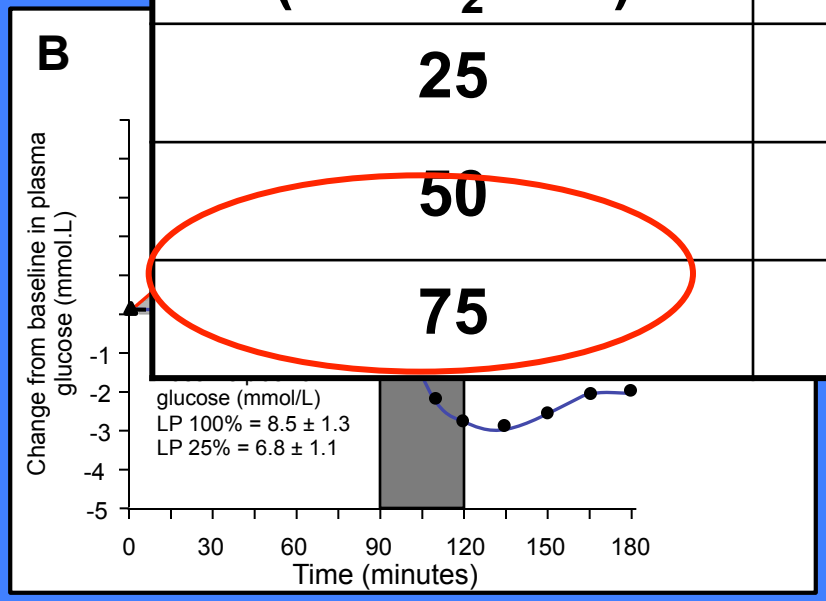


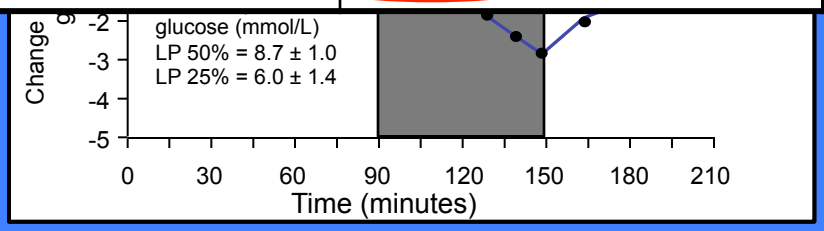
Insulin dose adjustment





	% Dose reduction	% Dose reduction
Exercise intensity (% VO_2max)	**30 min of exercise**	**60 min of exercise**
25	25	50
50	50	75
75	75	-

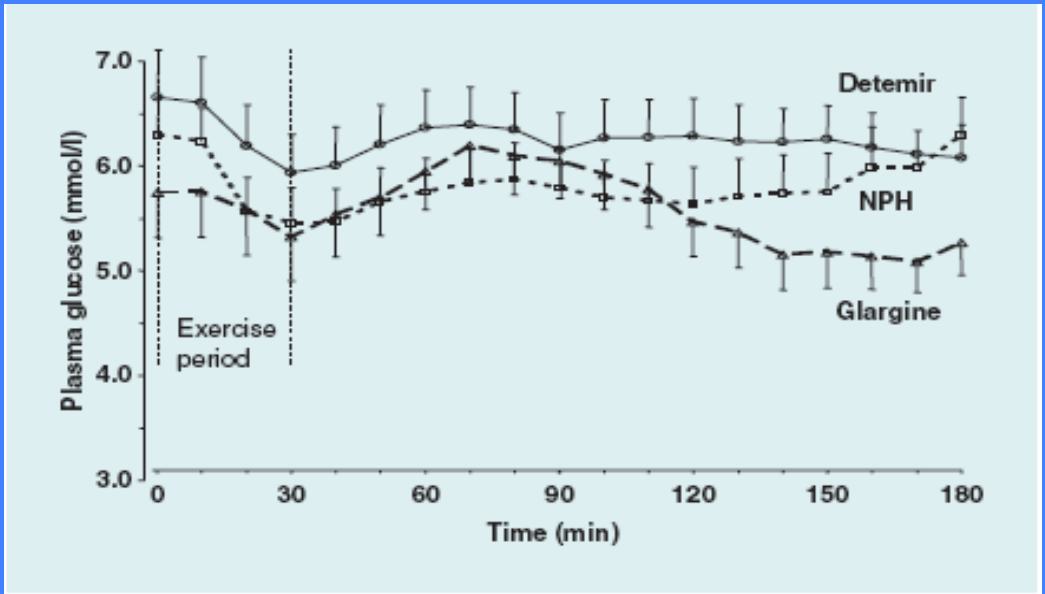


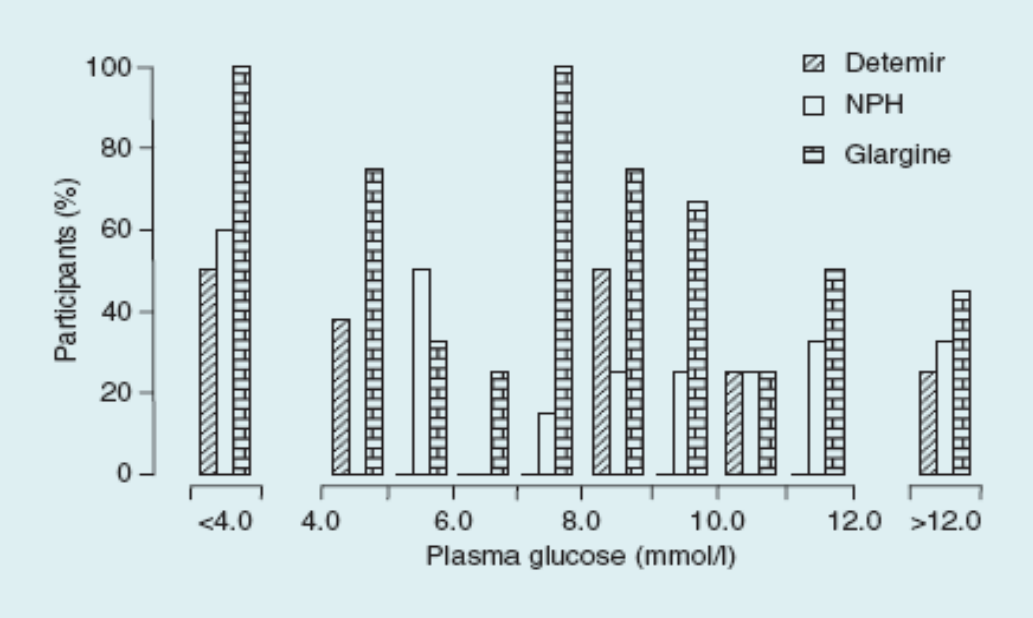


Data are means ± SEM; *p<0.05 by repeated measures using ANOVA; LP: lispro.

Rabasa-Lhoret R et al. *Diabetes Care.* 2001;**24**:625–630.

Hypoglycaemia seems to be more common with Glargine than either NPH or Detemir



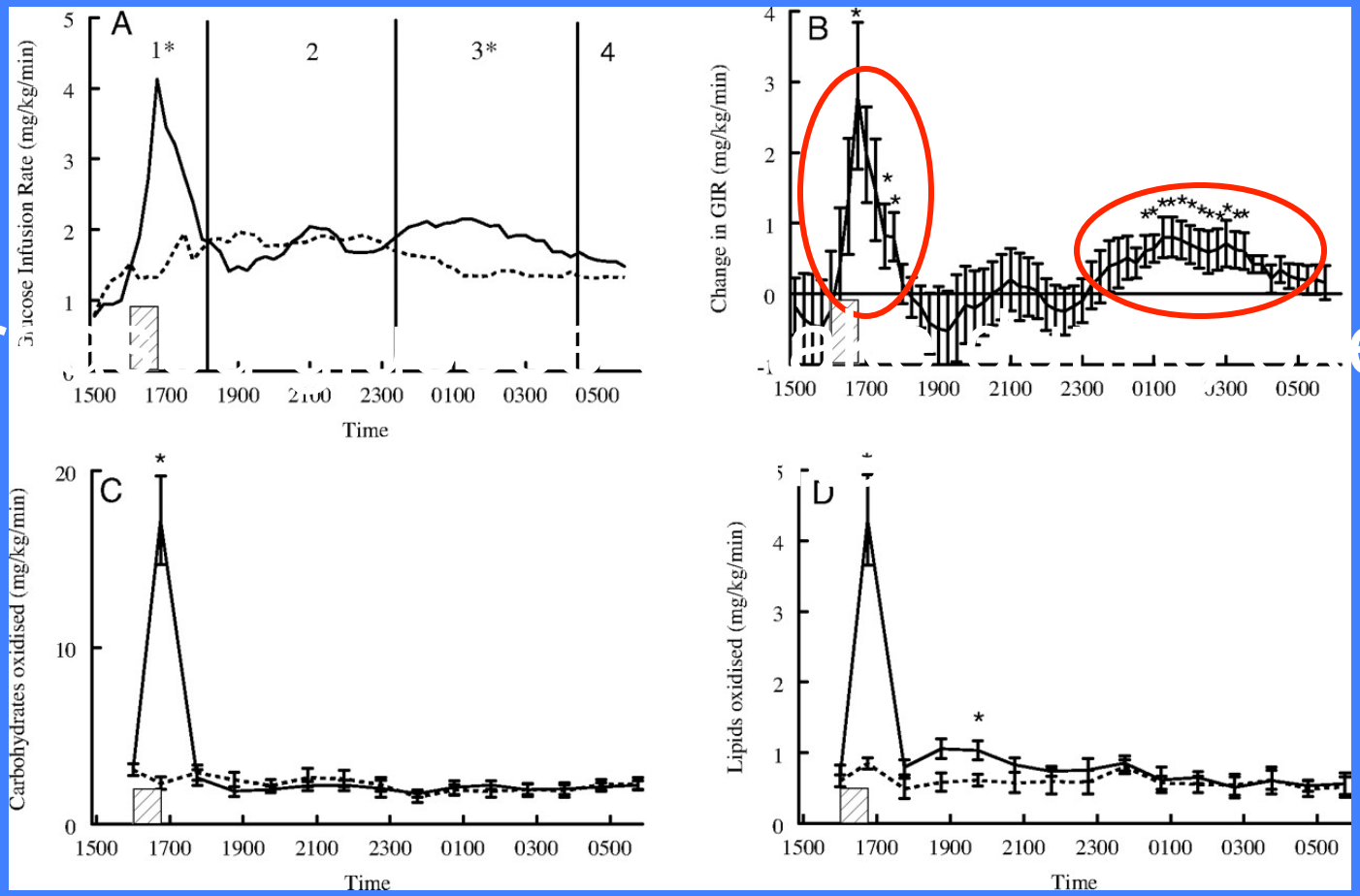


Diabetic Medicine, **26**, 1027–1032

Nocturnal hypoglycaemia

Biphasic response in glucose requirement with exercise

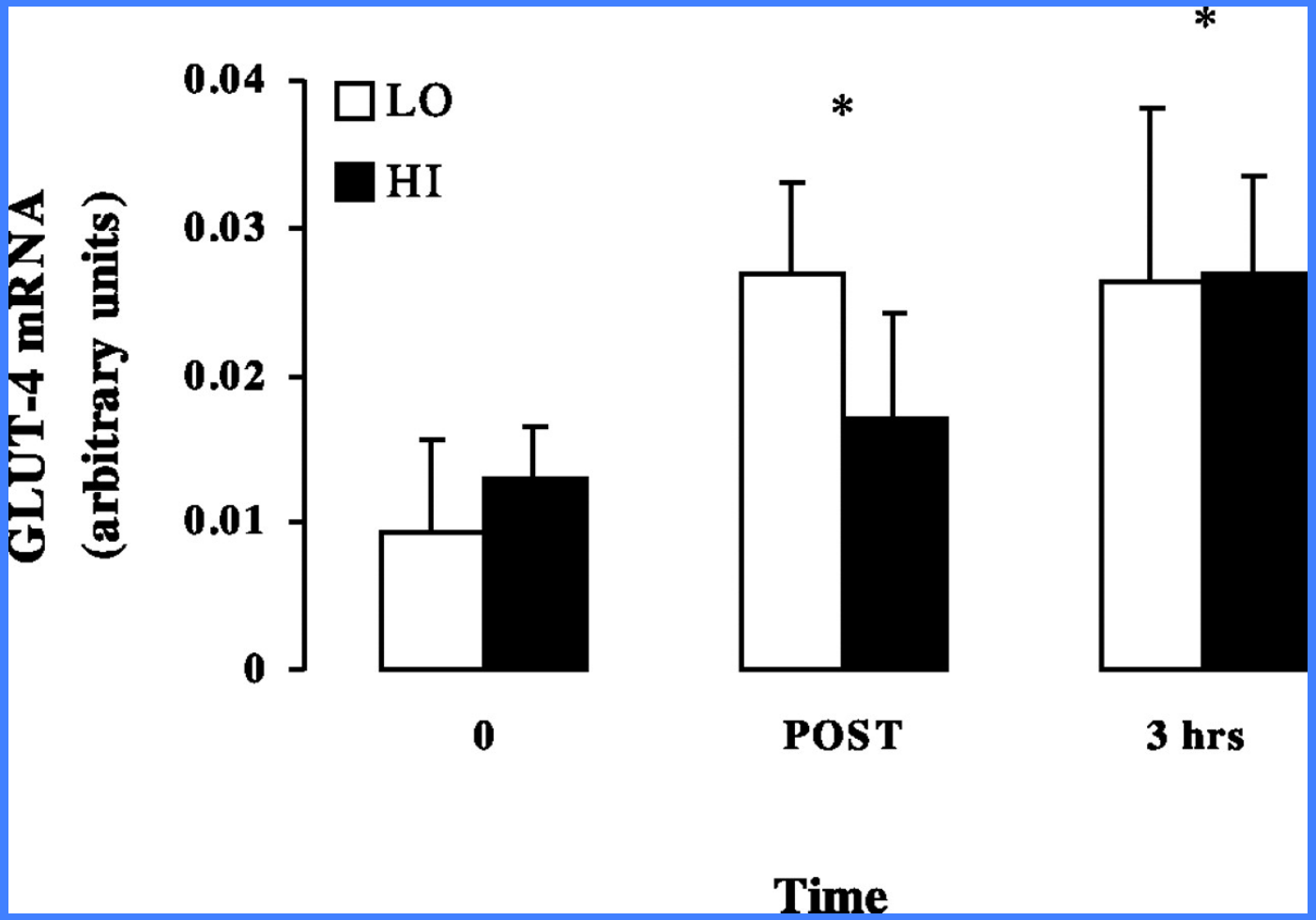
Incr ercise,



Responses of glucose infusion rate (mg/kg{middle dot}min) (A), difference in glucose infusion rate (GIR) between exercise and rest studies (mg/kg{middle dot}min) (B), rate of carbohydrate oxidation (mg/kg{middle dot}min) (C), and rate of lipid oxidation (D) to exercise (solid lines) and rest (dashed lines) studies

McMahon, S. K. et al. J Clin Endocrinol Metab 2007;92:963-968

Skeletal muscle GLUT-4 gene expression before (0), immediately after (Post), and 3 h after (3 hrs) exercise at ~40% (Lo) or ~80% (Hi) peak pulmonary oxygen consumption



Kraniou, G. N. et al. J Appl Physiol 101: 934-937 2006;
doi:10.1152/japplphysiol.01489.2005

Journal of
Applied Physiology

Delayed hypoglycaemia CGMS following exercise in T1DM

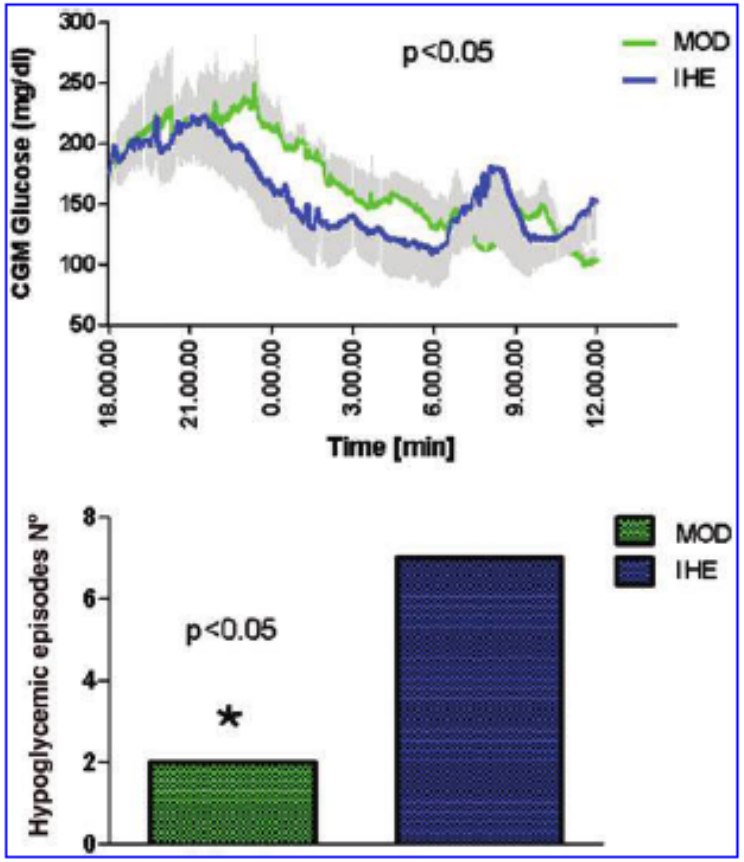


FIG. 4. Interstitial plasma glucose assessed by continuous glucose monitoring (CGM) (**upper panel**) and of hypoglycemic episodes during moderate intensity exercise (**lower panel**) after moderate-intensity exercise (MOD) (green line/bar) and during intermittent high-intensity exercise (IHE) (blue line/bar). Data are mean ± SEM values. Color images available online at www.liebertonline/dia.

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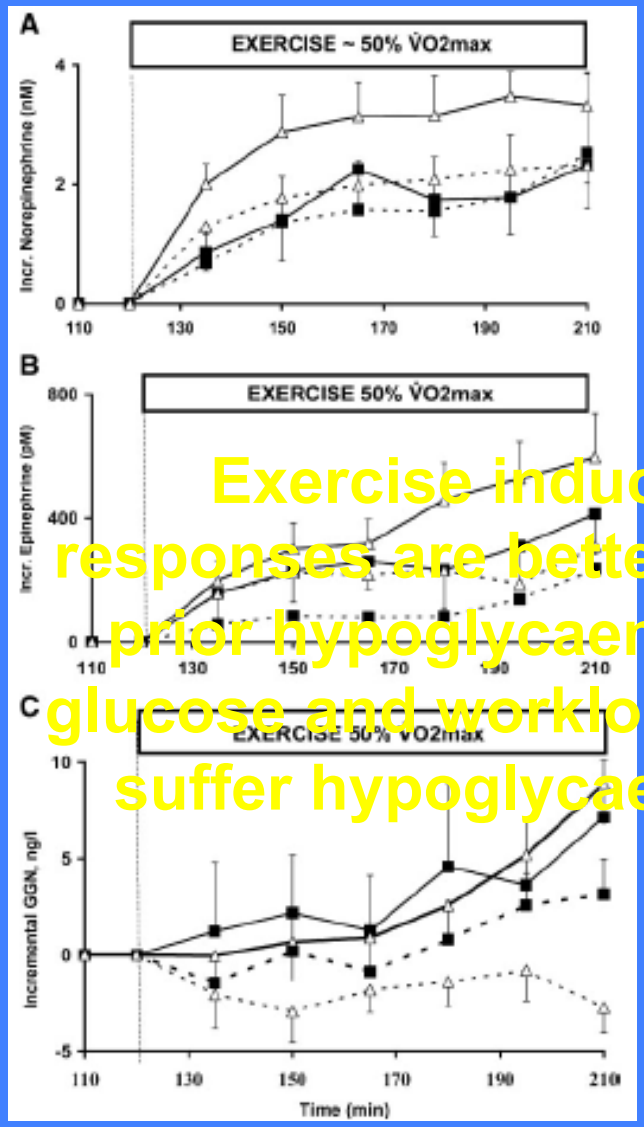
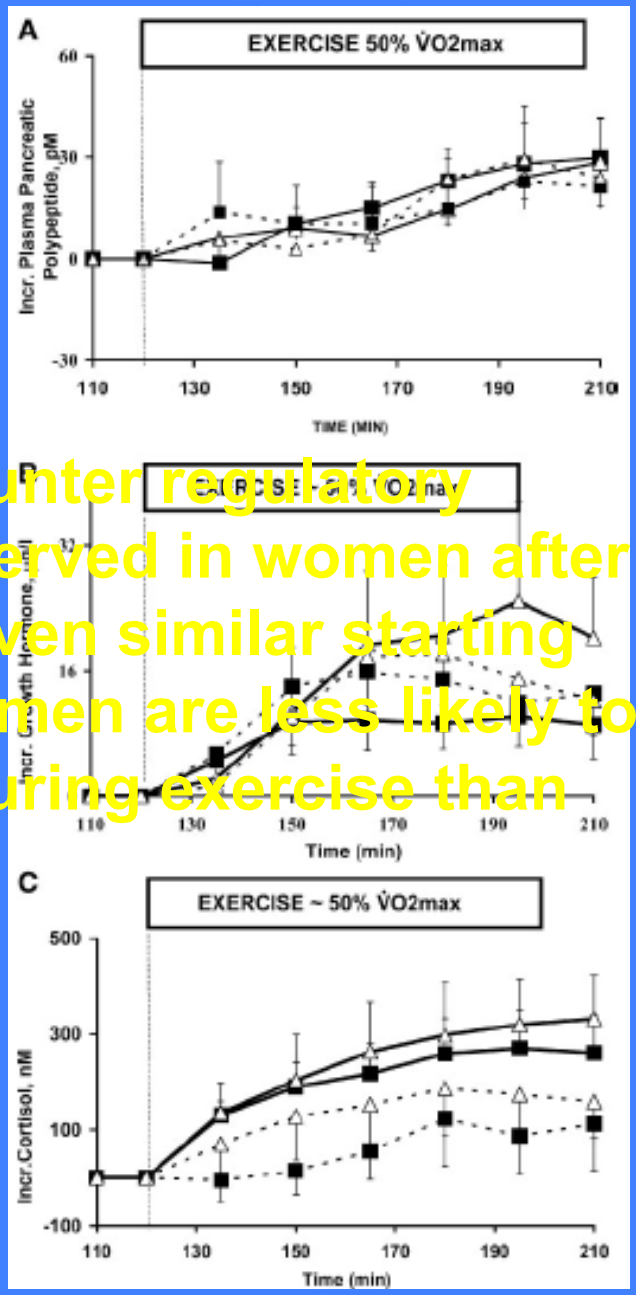
Volume 12, Number 10, 2010





F ante eugly
M ante eugly
F ante hypo
M ante hypo

Am J Physiol Endocrinol Metab 287: E16–E24, 2004.

Exercise induced counter regulatory responses are better preserved in women after prior hypoglycaemia. Given similar starting glucose and workload, women are less likely to suffer hypoglycaemia during exercise than men

The complex interaction between hypoglycaemia and exercise

- Exercise markedly increases muscle insulin sensitivity by increasing GLUT4 transporters[1]
  - Effect from 6-12 hours post exercise lasting 48 hours.
- Prior hypoglycaemia impairs counter-regulatory response to exercise, and this is proportional to the level of hypoglycaemia[2].
- Prior exercise impairs the counter-regulatory response to hypoglycaemia[2].
- The counter-regulatory response to exercise is relatively preserved in women following hypoglycaemia[3].

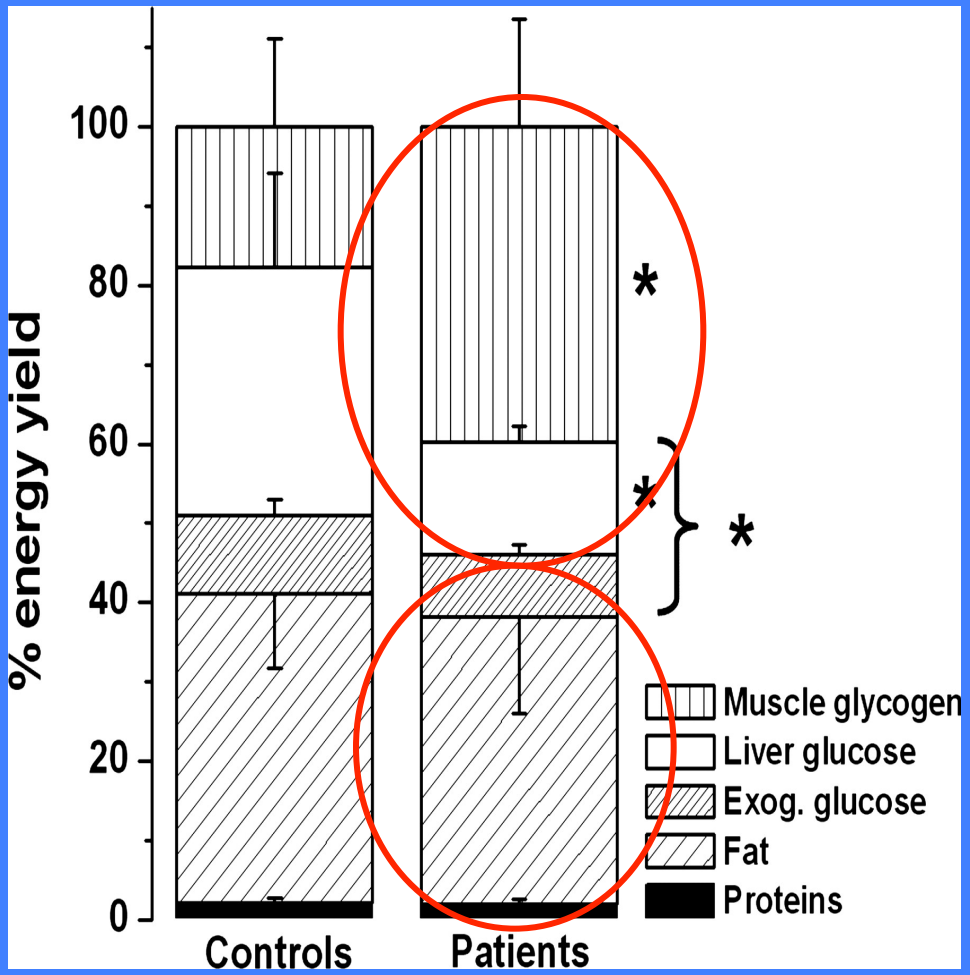
- 1 Thorell A, Hirshman MF, Nygren J et al. Exercise and insulin cause GLUT-4 translocation in human skeletal muscle. Am J Physiol Endocrinol Metab 1999;277:E733-41.

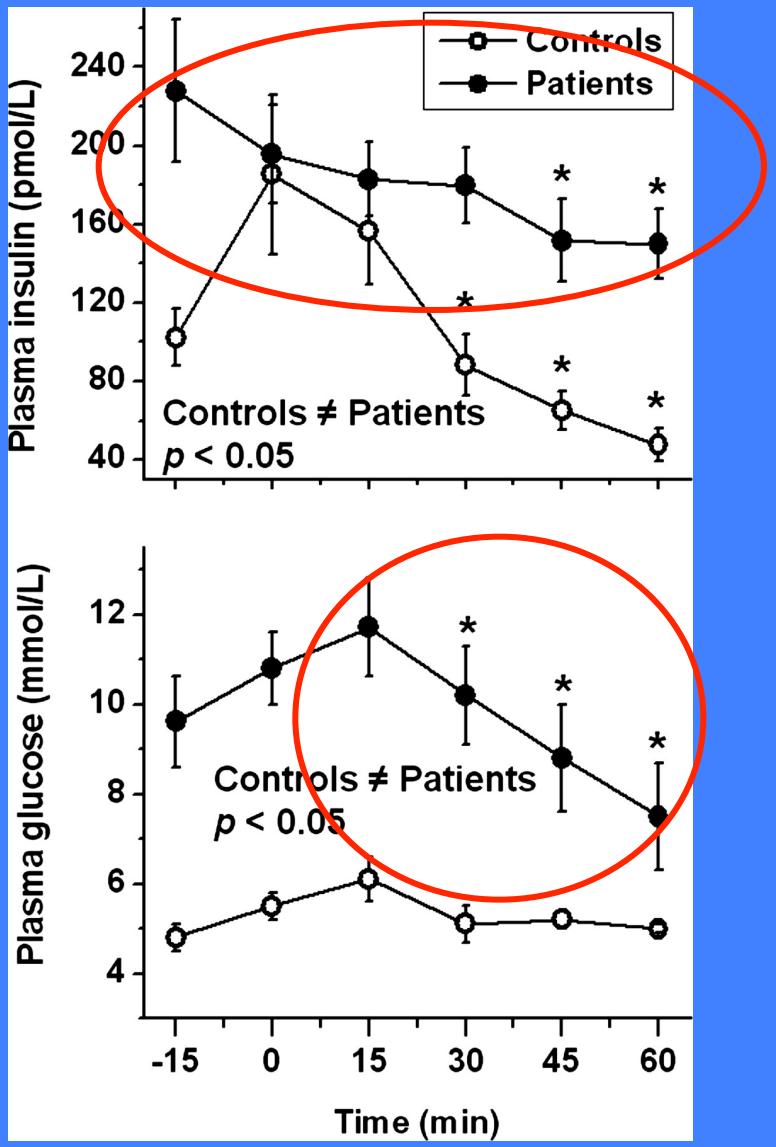
2 Galassetti P, Tate D, Neill RA et al. Effect of antecedent hypoglycaemia on counterregulatory responses to subsequent euglycaemic exercise in type 1 diabetes. Diabetes 2003;52:1761-9.

3 Galassetti,P.; Tate,D.; Neill,R.A.; Morrey,S.; Wasserman,D.H.; Davis,S.N. Effect of sex on counterregulatory responses to exercise after antecedent hypoglycemia in type 1 diabetesAmerican Journal of Physiology - Endocrinology & Metabolism.2004, 287(1):E16-24,

Fatigue

Fuel oxidation in T1DM





Robitaille M et al. J Appl Physiol 2007;103:119-124

Fuel metabolism during exercise in euglycaemia and hyperglycaemia in patients with type 1 diabetes

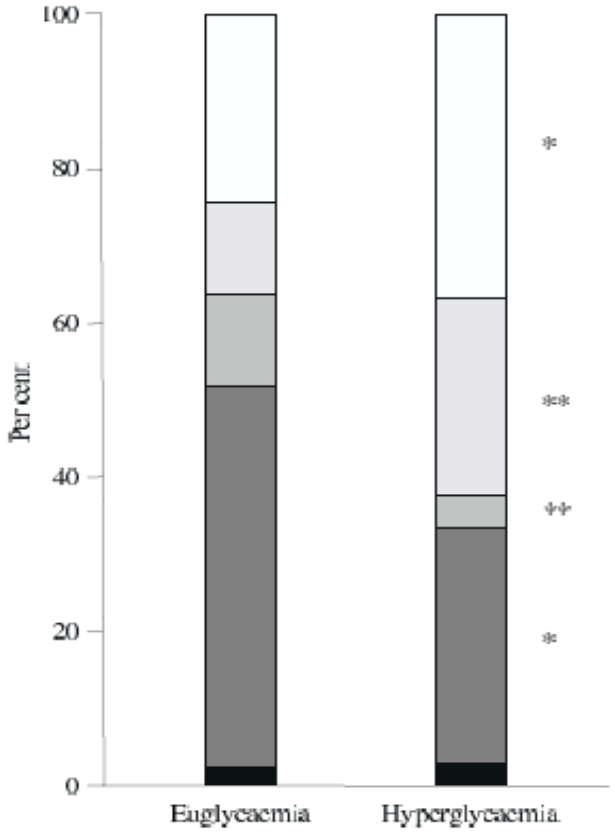


Fig. 4 Relative energy contribution of specific substrates at the end of exercise during euglycaemia and hyperglycaemia. Data are means (n= 7); *p<0.05 and **p<0.01 for comparison of corresponding energy substrates in euglycaemia and hyperglycaemia. White, glycogen; light grey, glucose infusion; medium grey, endogenous glucose; dark grey, lipids; black, protein

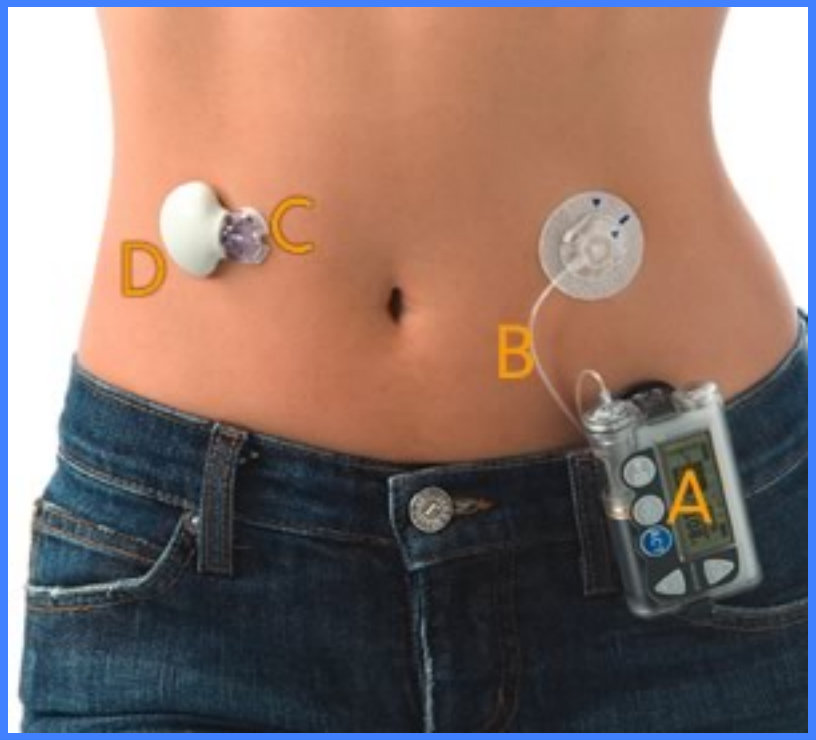
Diabetologia (2008) 51:1457–1465

Fatigue is common in diabetes - the role of fuel oxidation

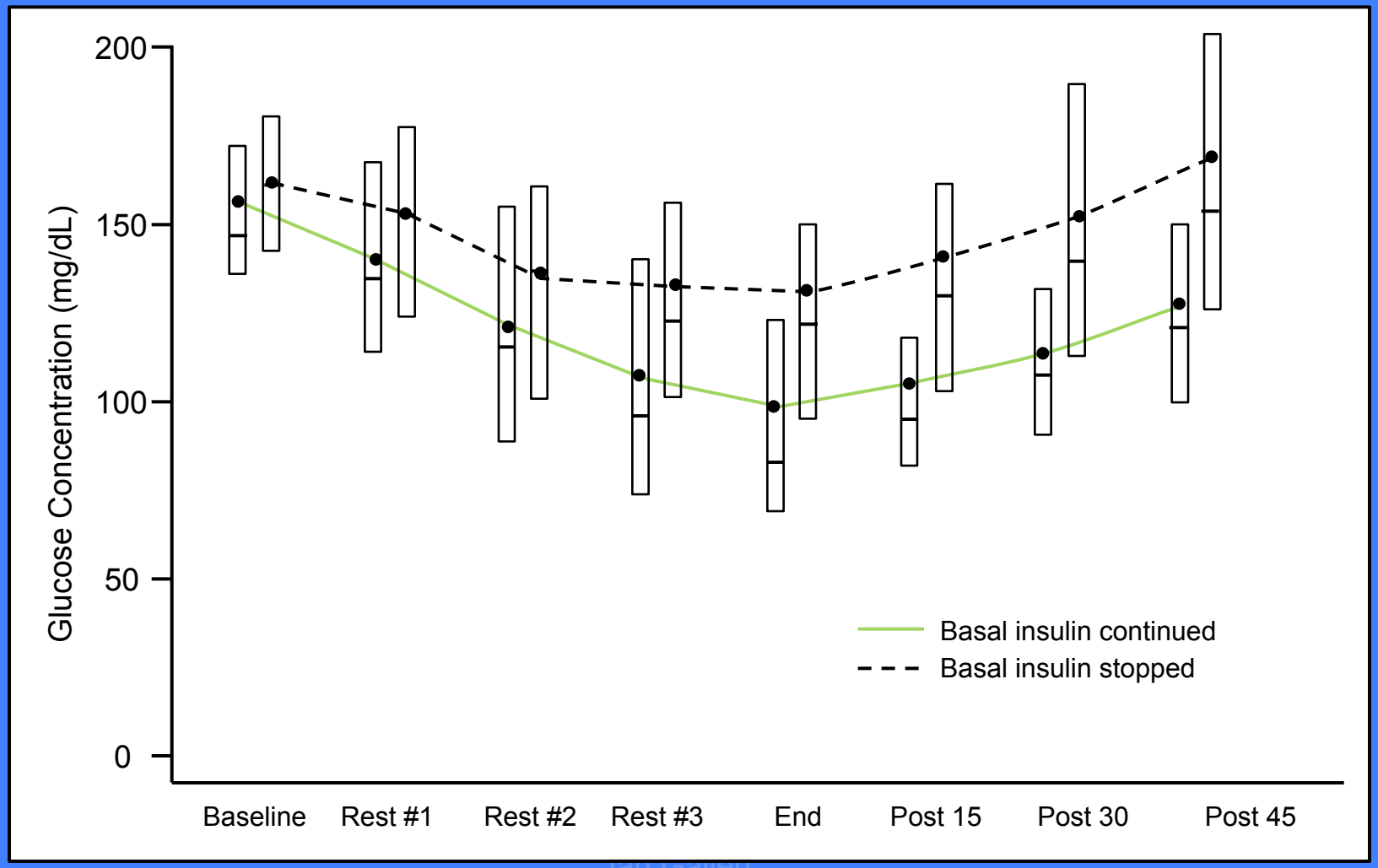
- Glucose oxidation is increased
- Endogenous hepatic glucose production is reduced
- Muscle glycogen mobilization and derived glucose oxidation increased
- Exogenous glucose oxidation in increased
- Glucose oxidation highest during hyperglycaemia

Insulin infusion pumps

- Enables normal basal insulin to be markedly reduced or suspended whist performing exercise.
- with rapid post exercise increase in insulin to deal with post exercise glycogenic peak.
- and lower post exercise nocturnal basal rate with intermittent exercise patterns.
- The gold standard for serious athletes where practical.



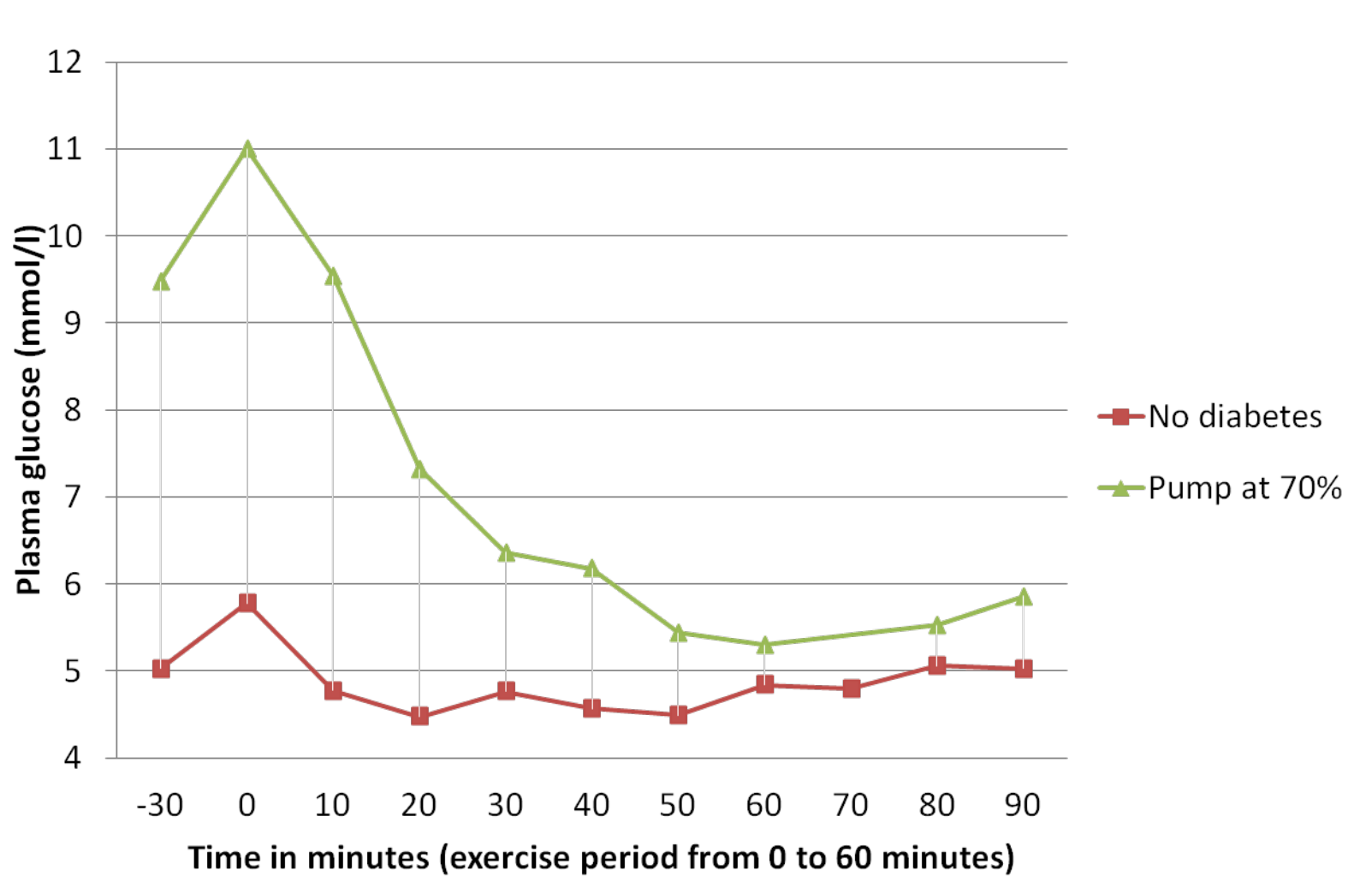
Prevention of Hypoglycemia During Exercise in Children With Type 1 Diabetes by Suspending Basal Insulin



Black dots denote mean values; Boxes denote median, and 25th and 75th percentiles.

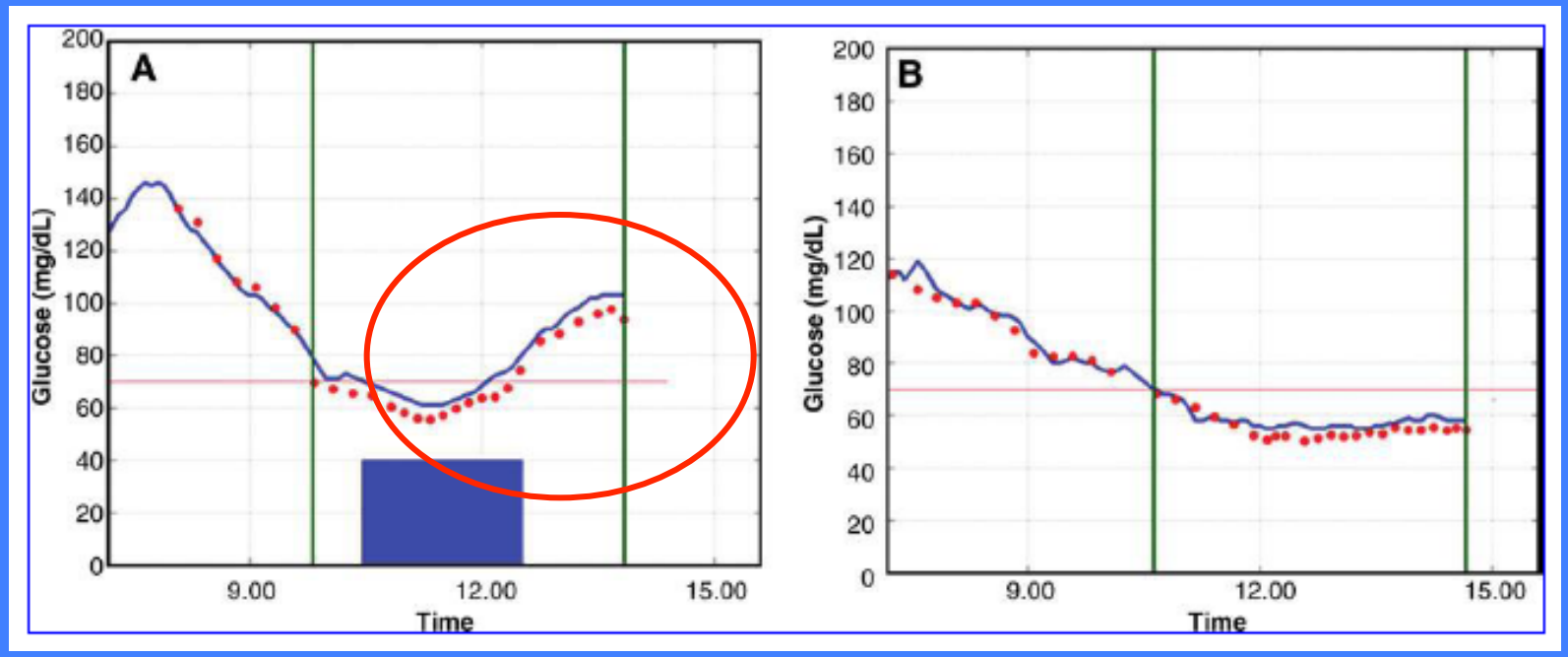
The Diabetes Research in Children Network. *Diabetes Care* 2006;**29**:2200–2204

Blood glucose with 1 hour of exercise at 50% VO_2 MAX



Progress towards an artificial Pancreas? Combination CSII/CGMS

Automatic low glucose infusion suspend during exercise



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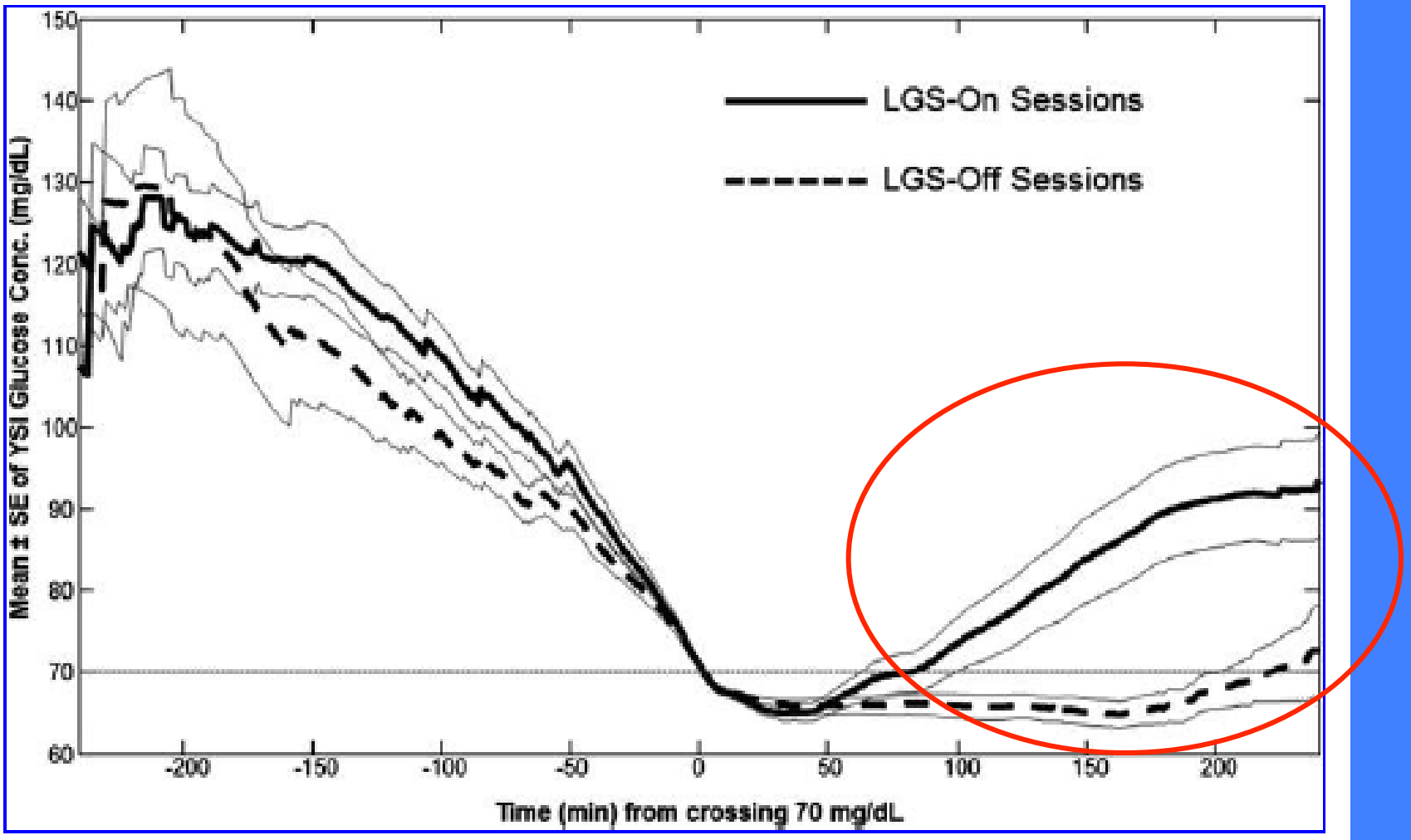
Automatic low glucose infusion suspend during exercise



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Are there any other strategies?

- Sympathomimetics
- Endogenous sympathetic stimulation

The 10-s Maximal Sprint:

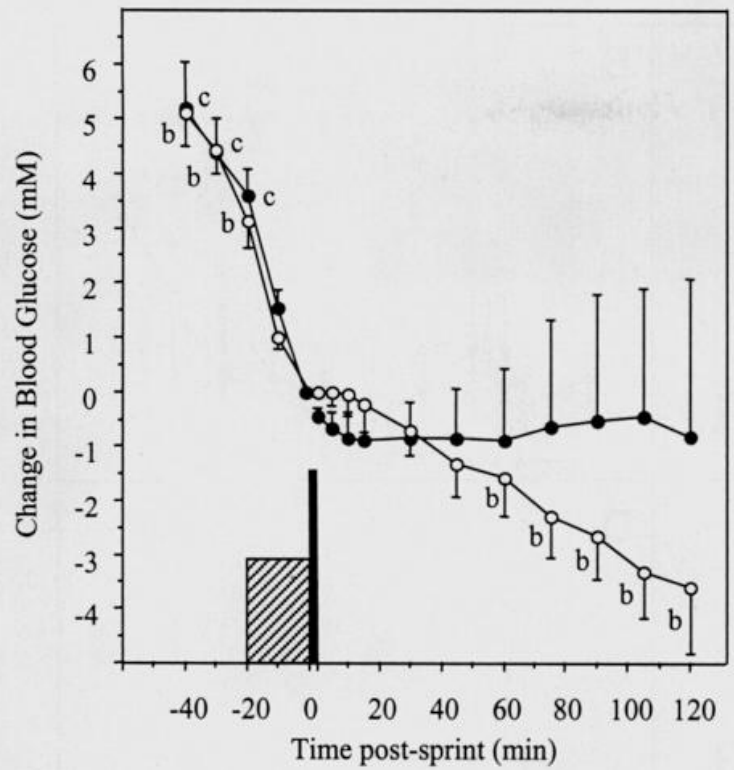
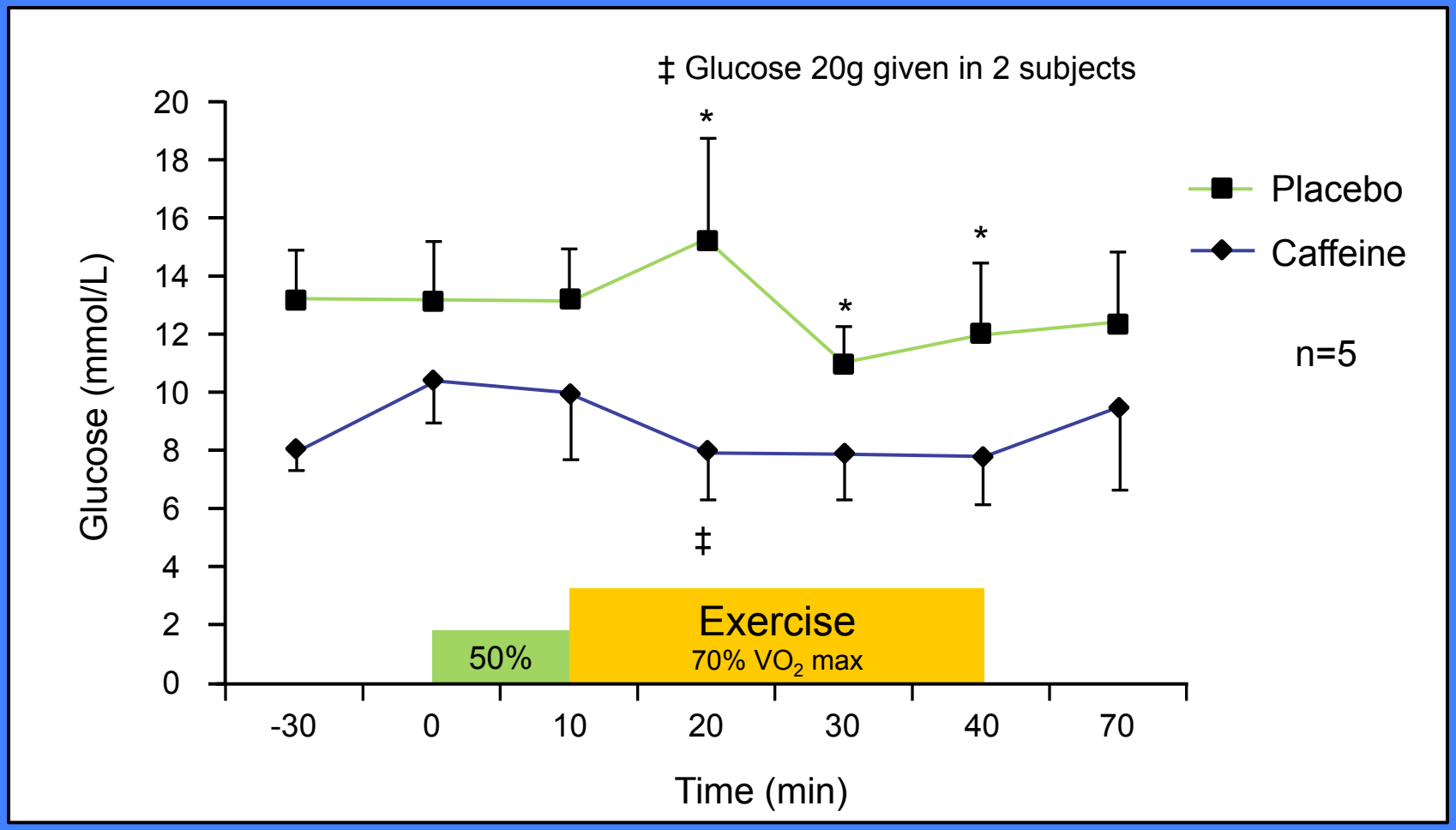


Figure 1—*Effect of a 10-s sprint on blood glucose after moderate-intensity exercise. The moderate-intensity exercise commenced at time point −20. Blood glucose levels are expressed relative to those immediately after the moderate-intensity exercise (time point = 0). All data are means ± SE. ▨, moderate-intensity exercise; vertical bar, sprint; ●, sprint trial; ○, control trial.* [b]*P < 0.05 vs. 0-min time point (after moderate-intensity exercise) in control trial;* [c]*P < 0.05 vs. 0-min time point (after moderate-intensity exercise) in sprint trial.*

Bussau, et al Diabetes Care. 2006. 29, 601.

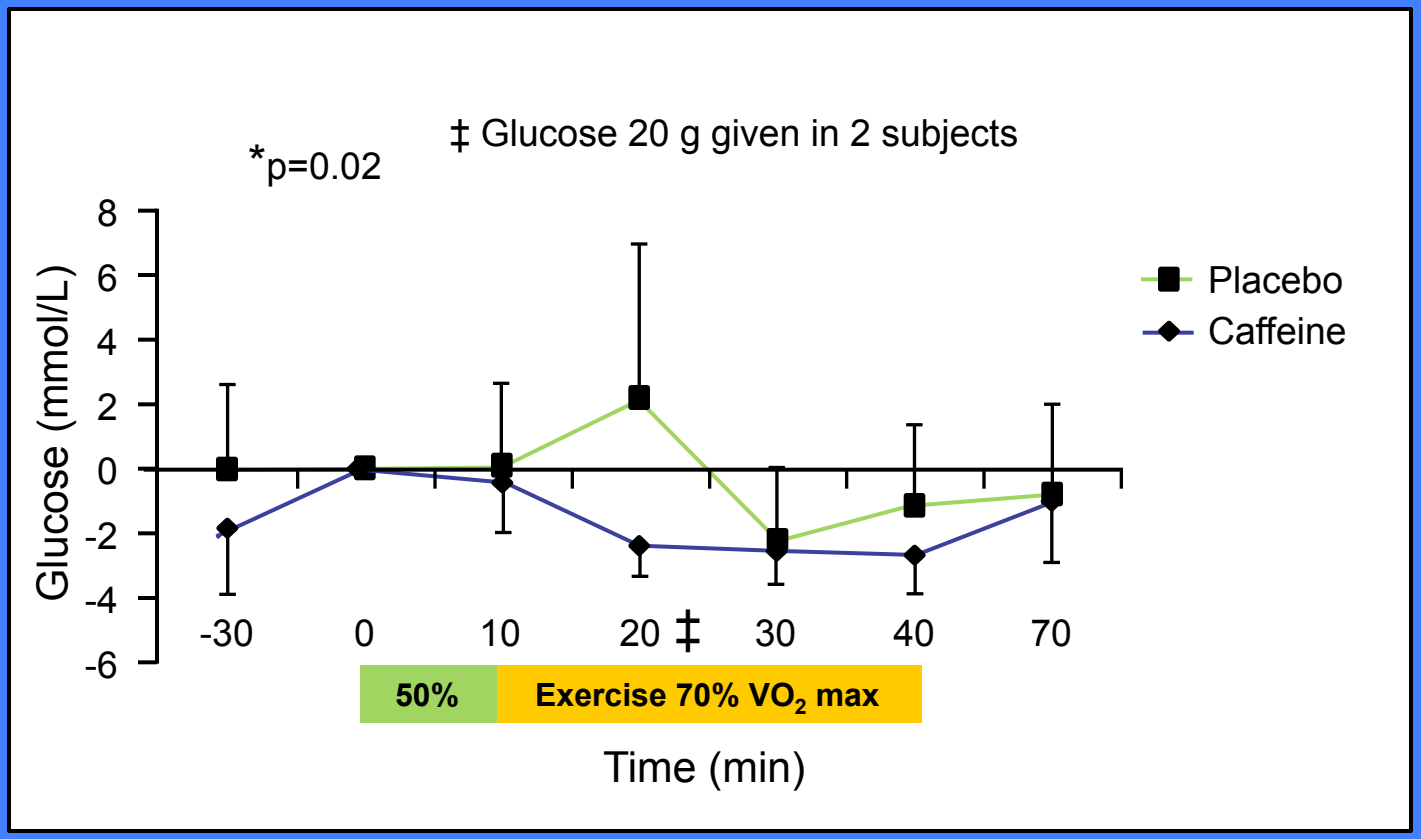
Caffeine (5mg/kg) and Blood Glucose During Prolonged Exercise



Ian Gallen

Gallen IW, et al. *Diabetes Care.* 2010;Abstract 1184−P

The Effect of Caffeine (5 mg/kg) on Blood Glucose During Prolonged Exercise



Ian Gallen

Gallen IW, et al. *Diabetes Care.* 2010;Abstract 1184−P

Score card at 10 years!

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Causes and treatment of fatigue	
How to use insulin pump treatment	

Summary of Clinical Strategies to Maintain Glycaemic Control With Exercise

Strategy	Advantages	Disadvantages
Reducing preexercise bolus insulin	Reduces hypoglycaemia during and following exercise; reduces CHO requirement	Needs preplanning; not helpful for spontaneous exercise or for late postprandial exercise
Reducing preexercise basal insulin	As above	As above, causes pre- and late postexercise hyperglycaemia
Taking extra CHO with exercise	Useful for unplanned or prolonged exercise	May not be possible with some exercises; not helpful where weight control important; easy to overreplace causing hyperglycaemia
Pre- or postsprint exercise burst	Reduces hypoglycaemia during and following sports	Effect limited to shorter and less intense exercise
Insulin pump therapy	Offers flexibility and rapid change in insulin infusion rates postexercise	Expensive; may not be practical for contact sports (eg, rugby/ football/ judo)
Reducing basal insulin postexercise	Reduces nocturnal hypoglycaemia	May cause morning hyperglycaemia

Lumb A., Gallen I.W. Curr. Opin. Endo. Diab and Obesity. 2009 16

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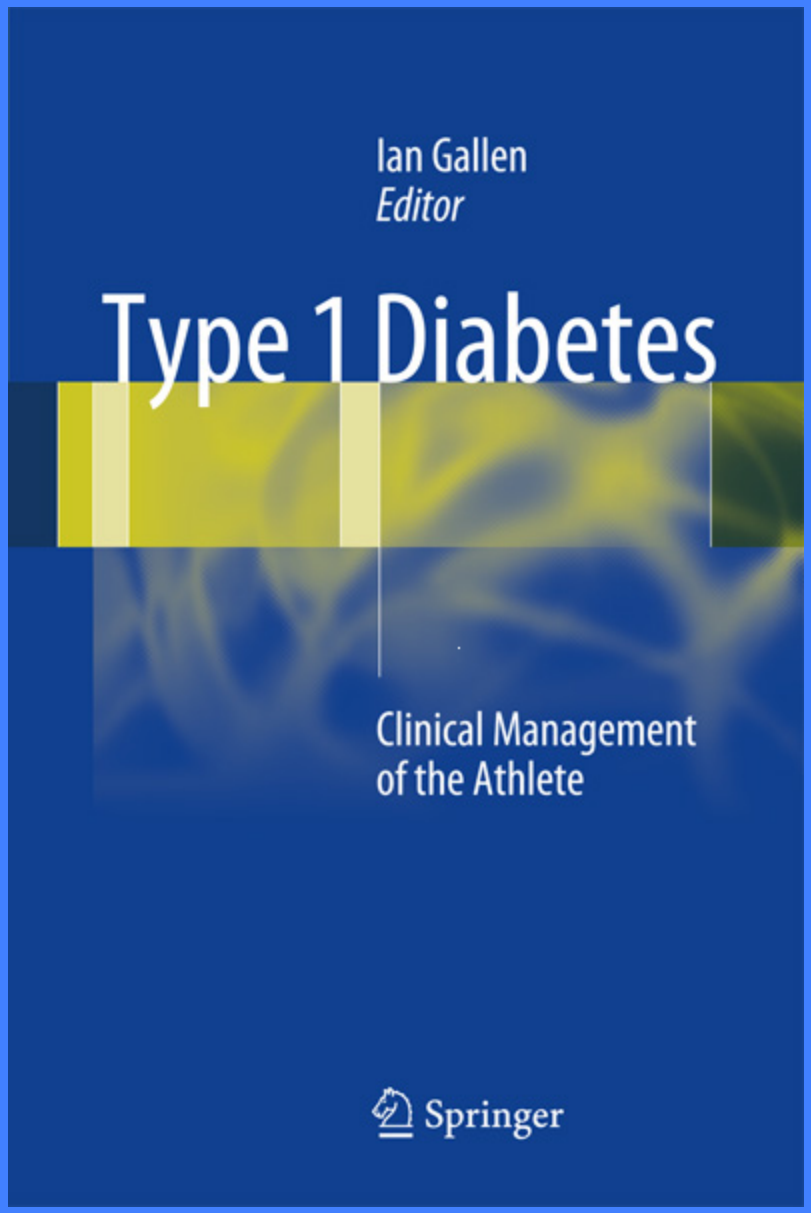
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