Basic science

DIABETES

Moderate exercise improves insulin sensitivity

Readability	✓ ✓
Applicability to practice	✓ ✓ ✓ ✓ ✓
WOW! factor	✓ ✓ ✓

1 The effects of moderate exercise training on peripheral glucose effectiveness, insulin sensitivity and endogenous glucose production (EGP) were studied using the stable-labelled, two-compartment, minimal model.

2 Seven men and one woman participated in cycle ergometer training at lactate threshold intensity for 60 minutes/day, 5 days/week for 12 weeks. Stable-labelled, frequently sampled, intravenous glucose tolerance tests were performed before, 16 h and 1 week after the last training session.

3 Peripheral glucose effectiveness and insulin sensitivity, analysed using the two-compartment minimal model, were significantly elevated 16 h after the last training session.

4 The elevated peripheral glucose effectiveness remained higher despite the cessation of exercise training for 1 week.

5 EGP was suppressed within 20 minutes after glucose bolus, and the suppression of EGP was followed by their overshoot. The time course of EGP during the intravenous glucose tolerance test remained similar after the training period.

6 Moderate exercise training at lactate threshold improves not only peripheral insulin sensitivity but also peripheral glucose effectiveness, with no change in the effect of glucose and/or insulin to suppress EGP in healthy humans.

Nishida Y, Tokuyama K, Nagasaka S (2004) Effect of moderate exercise training on peripheral glucose effectiveness, insulin sensitivity and endogenous glucose production in healthy humans estimated by a two-compartment-labelled minimal model. *Diabetes* **53**: 315–20

On your bike...increasing moderate exercise

Professor Adrian Bone, Head of Research, School of Pharmacy & Biomolecular Sciences, University of Brighton

The NSF for Diabetes confirms that type 2 diabetes is increasing markedly in the UK and, perhaps most worryingly, is becoming more frequent in young people. Fortunately, there are good indications that it may be possible to delay or even prevent the onset of disease. The reported benefits of regular exercise to people with diabetes include improvements in insulin sensitivity, glucose handling, lipid profiles and weight reduction. It is a popular misconception, however, that these types of health benefits can only be gained by the sort of regimens required in running the London Marathon or joining the SAS. Thus, it is very important that we develop a solid evidence base to show that even very moderate bouts of exercise (defined in the NSF as intensity sufficient to make you warm and breathe harder) taken regularly can be a very effective therapeutic tool in the prevention and treatment of type 2 diabetes. Exercise physiologists can provide this sort of information, and the paper by Nishida and colleagues serves as a useful example.

The present study seeks to clarify the effects of gentle exercise training on overall glycaemic control by monitoring both insulin action and insulin-independent glucose production. Using a stable isotope approach, the researchers were able to demonstrate that a 12-week exercise programme (at the lactate threshold) was able to produce significant improvements in both peripheral insulin sensitivity and glucose utilisation. These beneficial effects were observed without altering the ability of glucose and/or insulin to suppress endogenous glucose production. This is an important consideration as the hormonally-mediated adjustments necessary to maintain normoglycaemia during exercise are thought to be compromised in patients with either type 1 or type 2 diabetes.

The incidence of type 2 diabetes will continue to rise unless we are able to reverse the trends of decreasing physical activity and increasing levels of obesity. Exercise training must be evaluated like any other therapy but its potential for improving the major risk factors associated with diabetes and coronary heart disease is considerable.

DIABETES

Adipocyte hormones regulate energy intake

Readability	✓ ✓ ✓ ✓
Applicability to practice	✓ ✓
WOW! factor	✓ ✓ ✓ ✓

1 Hormones produced by adipose tissue play a critical role in the regulation of energy intake, expenditure and lipid and carbohydrate metabolism.

2 This review addressed the biology, actions and regulation of three adipocyte hormones, leptin, acylation-stimulating protein (ASP) and adiponectin.

3 Leptin production is primarily regulated by insulin-induced changes of adipocyte metabolism.

4 Dietary fat and fructose, which do not increase insulin secretion, lead to reduced leptin production, suggesting a mechanism for high-fat/high-sugar diets to increase energy intake and weight gain.

5 ASP increases the efficiency of triacylglycerol synthesis in adipocytes, leading to enhanced postprandial lipid clearance.

6 In mice, ASP deficiency results in reduced body fat, obesity resistance and improved insulin sensitivity.

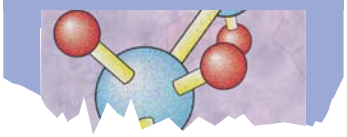
7 Adiponectin production is stimulated by thiazolidinedione agonists of peroxisome proliferator-activated receptor-γ and may contribute to increased insulin sensitivity.

8 These hormones are promising targets for managing obesity, hyperlipidaemia and insulin resistance.

Havel PJ (2004) Update on adipocyte hormones. *Diabetes* **53** (suppl 1): S143–51

'Autoantibody testing can identify a subgroup of relatives with an 89% risk of diabetes within 5 years.'

DIABETES



Islet autoantibody characteristics predict diabetes

Readability	✓ ✓ ✓
Applicability to practice	✓ ✓ ✓ ✓
WOW! factor	✓ ✓ ✓

1 Autoantibodies to islet cell antigens are the most widely used markers of pre-type 1 diabetes.

2 The risk of diabetes in relatives can be defined on the basis of the number of islet autoantibodies detected, together with first-phase insulin response to intravenous glucose.

3 This study has shown that the risk of diabetes can be further stratified if other islet autoantibody characteristics, including antibody titre, IgG subclass and/or positivity against the tyrosine phosphatase-like protein IA-2β, are also taken into consideration.

4 Autoantibody testing can identify a subgroup of relatives with an 89% risk of diabetes within 5 years.

Achenbach P, Warncke K, Reiter J et al (2004) Stratification of type 1 diabetes risk on the basis of islet autoantibody characteristics. *Diabetes* **53**: 384–92

ANNUAL REVIEW OF MEDICINE

β-cell replacement as an alternative to insulin therapy

Readability	✓ ✓ ✓
Applicability to practice	✓ ✓
WOW! factor	✓ ✓ ✓ ✓

1 The ability to achieve insulin independence with either solid-organ pancreas or islet transplantation has increased the number of patients seeking β-cell replacement as an alternative to insulin therapy.

2 Pancreatic islet transplantation provides a safer and less invasive alternative for β-cell replacement that could be justified earlier in the course of diabetes to prevent secondary complications.

3 The widespread application of islet transplantation will depend on further improvements in selective immunosuppression, development of immunologic tolerance and finding new sources of β cells.

Stock PG, Bluestone JA (2004) Beta-cell replacement for type 1 diabetes. *Annual Review of Medicine* **55**: 133–56

OBESITY RESEARCH

Insulin action on expression of novel adipose genes

Readability	✓ ✓ ✓
Applicability to practice	✓ ✓ ✓
WOW! factor	✓ ✓ ✓ ✓

1 Adipose tissue secretes several molecules that may participate in metabolic cross-talk to other insulin-sensitive tissues.

2 The authors studied the expression and acute insulin regulation of novel genes expressed in adipose tissue that are implicated in the control of whole-body insulin sensitivity.

3 The expression of adiponectin, c-Cbl-associated protein (CAP), 11β hydroxy-steroid dehydrogenase type 1 (11β-HSD-1) and sterol regulatory element-binding protein (SREBP)-1c was determined in subcutaneous adipose tissue from men with type 2 diabetes.

4 Expression of adiponectin, CAP, 11β-HSD-1 and SREBP-1c was similar between healthy men and those with type 2 diabetes.

5 Insulin infusion for 3 h did not affect expression of CAP, 11β-HSD-1 or adiponectin mRNA in either group. However, insulin infusion increased SREBP-1c expression by 80% in healthy men, but not in those with type 2 diabetes.

6 The results provide evidence that insulin action on SREBP-1c is dysregulated in adipose tissue from people with type 2 diabetes.

7 Impaired insulin regulation may contribute to the pathogenesis of type 2 diabetes.

Koistinen HA, Forsgren M, Wallberg-Henriksson H, Zierath JR (2004) Insulin action on expression of novel adipose genes in healthy and type 2 diabetic subjects. *Obesity Research* **12**: 25–31

'Angiotensin-II antagonists (AIIAS), such as losartan, represent the only evidence-based treatment strategy for patients with type 2 diabetes and proteinuria.'

CLINICAL THERAPEUTICS

Angiotensin-II antagonists delay nephropathy

Readability	✓ ✓
Applicability to practice	✓ ✓ ✓ ✓ ✓
WOW! factor	✓ ✓

1 Preventing or delaying the progression of renal disease from microalbuminuria to nephropathy and, ultimately, to end-stage renal disease is a crucial goal of diabetes management.

2 A MEDLINE search was used to gather articles on the management of type 2 diabetes published between 1999–2003.

3 Angiotensin-II antagonists (AIIAs), such as losartan, represent the only evidence-based treatment strategy for patients with type 2 diabetes and proteinuria.

4 AIIAS, such as losartan, should be considered mandatory therapy in patients with diabetic nephropathy and should complement existing management strategies, such as reduced dietary protein intake, strict blood glucose control and standard antihypertensive therapy.

Ruilope LM, Segura J (2003) Losartan and other angiotensin II antagonists for nephropathy in type 2 diabetes mellitus: a review of the clinical trial evidence. *Clinical Therapeutics* **25**: 3044–64