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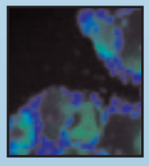


Steps towards gene therapy in diabetes

By James Shaw
Senior Lecturer and Honorary Consultant in Diabetes, University of Newcastle
and Stijn Niessen
Research Fellow, Royal Veterinary College, London

What is gene therapy?

The genes which we inherit from our parents are stored within the cells making up all of our organs and tissues. Each gene contains a DNA code which forms the template for RNA messages which leave the nucleus and direct construction of specific proteins. Proteins form the building blocks and control key chemical reactions determining the structure and functions of each cell.

Gene therapy comprises the introduction of new genes into cells or modification of existing genes to treat or prevent disease.

This form of treatment is particularly promising for conditions caused by an inherited abnormality in a single gene. These include haemophilia, muscular dystrophy and cystic fibrosis. Haemophilia, a bleeding disorder caused by a congenital deficiency of a clotting factor, is an example where scientists have made great progress using gene therapy. Complete cures have been achieved in animal studies with one of the first human recipients showing short-term improvement.

What does gene therapy involve?

Techniques include the transfer of genes directly to an individual (for instance via an injection into muscle or an organ such as the liver) or initially to cells or organs outside the body, with subsequent transplantation. The cells can be obtained from the recipient themselves or from living or deceased human donors, animal donors, or modified cell lines. The new genes are incorporated into carriers (known as vectors) which help transport them into the cell nucleus and enable efficient

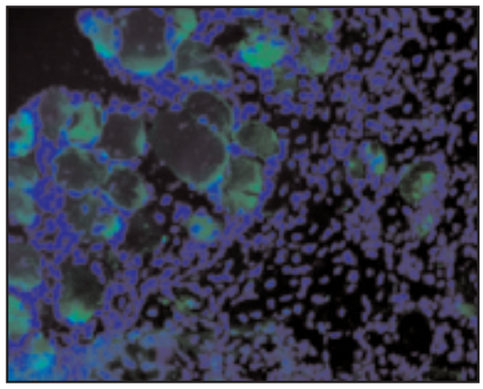


Figure 1. Green staining of insulin produced in muscle at 1 week following simple intramuscular injection of an insulin gene.

synthesis of the therapeutic proteins using the cell's own machinery.

The majority of clinical gene therapy trials to date have been undertaken in individuals with malignant disease and have used viral vectors. Viral vectors are modified and deactivated viruses capitalising on the incredible efficiency with which different viruses are able to enter, survive and function in human cells.

What are possible problems?

There are many different types of viral vectors each with potential advantages and disadvantages. The best choice depends on the particular requirements for each gene therapy application. Clinical success has been realised using vectors derived from retroviruses to deliver a normal copy of an abnormal gene in the white blood cells (the body's immune system cells) of patients with severe inherited immune deficiency. However, incorporation of the vector into the white blood cell chromosomes led to two cases of leukaemia (cancerous changes in the blood cells) in the first ten children treated.

In addition, over thousands of years our immune system has developed specific

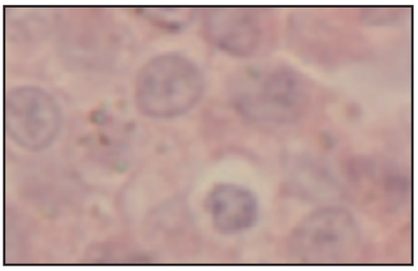
Continued on page 6

New research moves pancreatic cell transplants a step closer

US Researchers working towards a cure for diabetes using pancreatic cell transplants have taken a step closer in dealing with immune rejection according to a new study.

The researchers from Albert Einstein College of Medicine of Yeshiva University engineered insulin producing beta cells which contained genes from a virus capable of evading detection by the body's immune system. These were then transplanted into mice with diabetes.

In the mice injected with the modified cells, normal glucose control was achieved for up to three months. Normally transplanted cells are able to restore normal glucose control but are destroyed by the body in a few days. Because of this and the toxic effects caused by the immunosuppressant drugs used to prevent rejection, this type of cell transplantation therapy has always been limited.



The insulin producing beta cells

The researchers are now looking at other viral genes that also contribute to immune suppression in order to find the best gene combination to use to combat rejection.This research is in its very early stages.

Diabetes drugs and possible bone fracture risk

Thiazolidinediones may increase the risk of bone fractures in some groups of women, more research is needed

New research carried out by British and American scientists claims that the long term use of Thiazolidinediones, used to treat type 2 diabetes, could double the risk of some women breaking bones.

The researchers from the University of East Anglia and Wake Forest University, North Carolina in the US analysed the findings of ten studies involving at least 14,000 people with type 2 diabetes.

They compared the bone health of people who were on the drugs and those who were not. The study showed that the use of Thiazolidinediones affected bone density in the spine and at the hip in some women, it showed no increased fracture risk in men.

It should be emphasised that an increased risk in bone fractures is only applicable to certain groups of women. More evidence is needed before a conclusive link is drawn.

Both the MHRA and the European Medicines Agency advise that people taking Thiazolidinediones, more commonly know as Glitazones, should not stop taking their medication. If individual's are worried they should consult their doctor.

News update

First trial of insulin produced in plants takes place in UK

The world's first trial of human insulin produced in plants is underway in the UK. It is hoped that this could be a new source of insulin which will help meet growing demand as diabetes prevalence increases.

A genetically modified variety of safflower that makes high concentrations of human insulin has been developed by SemBioSys, a Canadian biotechnology company. Safflower is currently a minor source of seed oil from which insulin can be easily extracted.

The trial will show whether human insulin derived from the safflower plant has the same effects on blood sugar levels as commercial human insulin, which is largely produced by cultures of genetically engineered bacteria in huge fermenters.

Thirty healthy volunteers are taking part in the trial, which if successful, will be extensively tested with people with diabetes.

The cost of producing insulin using

Biopharming uses genetically engineered crops to produce different types of human molecules

'bio-pharming' methods, which aim to produce a range of human molecules in genetically engineered plants, is 70 to 80 per cent lower than in bacterial fermenters say producer SemBioSys.

The plant produced insulin will need to undergo a demonstration of 'bio-equivalence' to prove that it is biologically identical to human insulin before seeking approval for sale from regulators such as the European Medicines Agency.

Watch this space for updates.

Sleep disorder and diabetes link

The melatonin receptor is the first gene to be linked to both high blood sugar and increased diabetes risk.

Scientists at the Oxford Centre for Diabetes have discovered a gene which links type 2 diabetes and sleep disorders according to a study recently published in *Nature Genetics*.

Results from the study point to a gene involved in detecting melatonin, a hormone that is responsible for sleep regulation, and an increased risk in diabetes.

Other genes have been linked to high levels of glucose in the blood, but the melatonin receptor is the first gene to be linked to both high blood sugar and increased diabetes risk.

The researchers looked at the genomes of over 36,000 people to look for changes associated with an increased risk of the condition and found a mutation in the MTNR1B gene, responsible for a 9 per cent increase in type 2 diabetes risk per copy of the mutated gene present.

It is hoped that the findings will help pave the way for a possible future genetic test to identify people that are at a higher risk of developing diabetes.

Three more genome studies were published in *Nature Genetics* which have investigated genes associated with heart disease, insulin levels, blood pressure and cholesterol.

News in brief

• Scientists estimate latest obesity figures

Scientists at University College Hospital in London have estimated that the obesity crisis will rise to 13 million people in the UK by 2012, with one in three adults being classed as clinically obese.

The researchers estimate that obesity costs the British economy between £6.6 and £7.4 billion each year. Estimations were based on annual data collected between 1993 and 2004 for the Health Survey for England, which looks at nearly 128,000 adults across the country.

• New cancer drug research shows promise for type 1

Researchers at the University of California have found that two common cancer drugs have been used to block and reverse type 1 diabetes in mice.

The findings of the study were published in *The Proceedings of the National Academy of Science*. The researchers, funded by the Juvenile Diabetes Research Foundation (JDRF), used Imatinib and Sunitinib to treat mice that are genetically engineered to be more susceptible to type 1 diabetes.

The cancer drugs block enzymes called tyrosine kinases that modify cellular signals and trigger growth. These enzymes are thought to play an important role in a number of conditions from cancer to type 1 diabetes.

The drugs were found to prevent the onset of the disease in the mice and in mice already with the condition, 80 per cent no longer had the condition after two months of treatment. This research is in its very early stages.

• New research claims pear shape less prone to diabetes

New research conducted by the Harvard Medical School on mice has laid claim to the fact that those with pear-shaped bodies, with fat deposits in the buttocks and hips, are less prone to type 2 diabetes and heart disease.

The team is trying to find the substances produced in fat that provide the protective qualities to use in the development of new drugs.

New and existing treatm

By Dr Sue Jones
Consultant Diabetologist, Institute
University Hospital of Hartlepool

Type 2 diabetes

Type 2 Diabetes (T2DM) is the commonest form of diabetes which, unlike Type 1 Diabetes, does not always require immediate treatment with insulin injections from diagnosis. T2DM is usually, but not inevitably, associated with obesity and many people have a family history of T2DM. The peak age for diagnosis of T2DM is over the age of 40 years but it can occur at younger ages, especially in overweight (Body Mass Index (BMI) of between 25.1 and 29.9 or obese, a BMI of greater than 30, or individuals with a family history of diabetes.

Treatments and newer agents

Treatments of T2DM are initially focused on lifestyle and dietary advice and people may be offered a structured education programme which should be seen as a vital part of diabetes treatment to understand about the condition, meet others with T2DM, and to learn how to get better control of diabetes. Dietary advice enables individuals to maintain or reduce weight, eat healthily, understand food labelling and plan meals. Diet and lifestyle modification advice is a lifelong part of T2DM treatment and tablets are in addition to this.

Tablets for T2DM are given at meal-times and include **metformin, sulfonylureas, acarbose and glitazones** which will each be discussed in turn. Newer treatments include tablets called **gliptins** and injections of **exenatide (Byetta®)**.

The newer agents are not suitable for everyone with T2DM and the indications for these treatments will be detailed below. Insulin is still required for people with T2DM and the indications for this will also be discussed. The majority of people with T2DM will be treated with a combination of two or more tablets. The tablets may be given in combination with insulin or exenatide aiming to achieve an HbA_{1c} (blood glucose control over the preceding 6 -8 weeks) below 7.5% and ideally between 6.5 - 7.0%. The HbA_{1c} target may actually be above 7.5% depending on circumstances and people with diabetes will have their individual target HbA1c set by their diabetes care team.

Metformin (Glucophage®)

Metformin (Glucophage®) is the commonest tablet used for treatment of T2DM and it does not cause hypoglycaemia (excessively low blood sugar levels) so blood glucose testing is not essential. Metformin reduces both the amount of glucose absorbed from the gut into the blood stream and glucose produced by the liver and promotes weight reduction. The latter makes it an ideal tablet for T2DM, as weight reduction is a key aim of treatment for the majority of people.

There are, however, a number of drawbacks to metformin and it cannot be used by people with kidney problems (creatinine levels above 150 μ mol. L^{-1}) or heart failure. The other major problems with metformin are diarrhoea, nausea and bloating (GI side effects) which can be very distressing. One strategy to minimise GI side effects is to start at low dose metfomin and gradually increase the number of tablets to the maximally tolerated dose. Unfortunately, many people are unable to achieve a high enough dose of metformin due to GI side effects and they should be offered a slow release preparation called **Glucophage SR®** which is a once or twice daily tablet which may be better tolerated. If GI side effects persist despite switching to **Glucophage SR®**, an alternative diabetes tablet will need to be considered.

Sulfonylureas (SUs)

Sulfonylureas (SUs) are first line treatment for people with T2DM who are not overweight or obese and for those people in whom metformin cannot be used.

There are a large number of SUs which are shown in **Table 1**. SUs make the pancreas produce more insulin so are associated with a risk of hypoglycaemia and people taking these tablets must be able to test their blood glucose levels. As SUs increase insulin production from the pancreas, they promote weight gain which is why they are not first line in overweight or obese people with T2DM. SUs are commonly added into metformin treatment when HbA1c rises above target.

Repaglinide (Prandin®) and **Netaglinide (Starlix®)** are short acting SUs-like tablets which can be used in those people in whom mealtimes vary dramatically, such as shift workers, but they are not widely used. Both of these tablets are associated with a risk of hypoglycaemia so people taking these must be able to test their blood glucose levels.

Acarbose

(Glucobay®) is a tablet that works by reducing the amount of glucose absorbed by the gut and is given three times a day. Due to its mode of action, it has major GI side effects which limit its use as many people cannot reach the recommended dose of 100mg three times a day. It can be used as an alternative to metformin in people with heart failure or kidney problems, but is not a very strong tablet and usually has to be combined with other tablets to control diabetes.

Glitazones

Glitazones are a unique type of diabetes tablet which increase the ability of the body to use its own insulin. The majority of people with T2DM have a condition called insulin resistance, which means that they are able to make insulin from the pancreas, but they cannot use it correctly, and glitazones help to reduce insulin resistance. **Rosiglitiazone (Avandia®)** and **Pioglitazone (Actos®)** are the glitazones used in the UK and they are usually in combination with other diabetes tablets and are not first line for

Table 1: Sulfonylureas used in the UK

Generic Name	Trade Names	Frequency of administration
Gliclazide	Diamicron®	Once / twice daily
	Diamicron CR®	
Glipizide	Glibenese, Minodiab®	Twice Daily
Glimperide	Amaryl®	Once Daily
Tolbutamide		Twice / thrice daily
Glibenclamide*	Euglucon®	Once Daily

*Glibenclamide should be avoided in the elderly due to hypoglycaemia risk

nents for type 2 diabetes

the treatment of T2DM. Glitazones may be used in overweight and obese people with T2DM as an alternative to metformin or acarbose, as they are associated with less weight gain than SUs. Both rosiglitazone and pioglitazone are available in combination with metformin as **Avandamet®** and **Competact®** respectively. Glitazones cannot be used in people with heart failure or kidney problems and should be avoided in people with osteoporosis. Glitazones do not cause hypoglycaemia when used with metformin or acarbose, so blood glucose monitoring is not required, but people taking SUs and glitazones will have to test their blood glucose.

GLP-1 Analogues and Gliptins

GLP-1 Analogues and Gliptins are the latest treatments for T2DM and they make insulin work more efficiently. During a meal, food is absorbed from the gut and there is a rise in blood glucose which causes the pancreas to produce more insulin. This brings the blood glucose level down and enables the body to store the glucose for use later. In T2DM, the body is not able to produce insulin quickly enough and blood glucose remains too high after meals.

Studies in a desert lizard called a Gila Monster (pronounced 'Heela') have elucidated mechanisms by which insulin production is regulated by the body in response to a meal. The Gila Monster eats once or twice a year and is able to switch its insulin production on and off. Studies using extract of saliva from the lizard discovered that hormones called GLP-1 and DDP-4 control how insulin production is switched on and off.

GLP-1 like drugs (called analogues) have been developed the first of which is called **Exenatide (Byetta®)**. This has the ability to both increase insulin production in response to a meal and slow the rate at which the stomach empties. Exenatide is a fixed dose injection given under the skin twice a day using a disposable injection device.

Exenatide is currently only licensed for use in very obese people (with BMI's of over 35 and above) and cannot be used if there is a history of gallstones, excessive alcohol use or pancreatitis. It is essential that people on exenatide eat at least two meals per day, that the injection is given before eating and that the meals are eaten extremely slowly. Failure to comply with this will result in severe abdominal pain and vomiting. The majority of people on exenatide will demonstrate significant weight reduction but failure to reduce weight and / or improve HbA1c will necessitate discontinuation of the treatment as will severe abdominal pain. Exenatide is given in combination with metformin and / or SUs, but cannot be used with glitazones. It is not licensed for use in combination with insulin and very few patients will be able to switch from insulin to exenatide.

Gliptins

DDP-4 regulates the breakdown of GLP-1 so tablets called gliptins act on the DDP-4 receptor to slow the rate at which GLP-1 is broken down.

Sitagliptin (Januvia®) and **Vildagliptin (Galvus®)** are the two tablets available in the UK and are given once daily and cannot be prescribed without use of another diabetes tablet and are not licensed for use with insulin or exenatide.

Vildagliptin is also available as a combination tablet with metformin called **Eucreas**.

Diabetes and Insulin Therapy

By Sadie Cox, Diabetes Specialist Nurse

For people with Type 1 diabetes it is essential they commence insulin at diagnosis. They usually start on small doses of insulin and are given lots of support right from the beginning of diagnosis allowing them to master the technique of giving insulin.

As they require insulin 24 hours a day to maintain a healthy balanced metabolism - a regimen which mimics our normal body production of insulin is prescribed. This requires a long acting insulin which provides a 24 hour cover and is often known as the basal insulin or background insulin. However when they have food they may require a rapid acting insulin which works within a few minutes of injecting and is responsible for controlling glucose levels during and just after their meal.

For many people with Type 1 diabetes they require 4 or 5 injections a day with careful monitoring of glucose levels. It is for this reason that some people may choose to use an insulin pump which they wear 24 hours a day. The pump delivers a small dose of insulin continuously and when required they are able to inject extra units of insulin. Pump therapy still remains expensive in the UK and only a select number of people are able to make a choice to use this form of management for their diabetes.

People with Type 2 Diabetes may commence insulin but at a later stage of diagnosis. Insulin therapy is usually suggested where people are on maximum oral tablets and are having difficulty in controlling their blood glucose levels and/or having other complications relating to diabetes.

Most commonly people with Type 2 diabetes commence on a daily injection of a long acting insulin which addresses some insulin resistance and continuous high glucose levels. It may be over time they have to introduce a rapid or short acting insulin to manage post prandial peaks or commonly known as raised glucose levels after meals.

There are a wide range of different types of insulin which are used in combination - each having their own start time and length of action. It is for this reason that insulin therapy has remained a specialist skill in a hospital setting.

However with the introduction of a once a day 24 hour peakless insulin (which is less likely to cause hypo's) and the increasing need to support people with Type 2 Diabetes with insulin therapy, this has developed skills out in the community where more people are now being managed appropriately on insulin therapy through their Practice Nurse and General Practitioner.

Diabetes is a difficult disease to manage - it is progressive and ever changing. It is impossible to treat everyone in the same way. One of the essential elements is that each person has an opportunity to discuss their lifestyle, their needs and fears.

Steps towards gene therapy in diabetes

Continued from page 1
strategies to eliminate viral infections, with the potential of immune rejection and inflammatory response to gene therapy vectors including viral components. A further danger is that the viral vector may regain the ability to replicate, causing a genuine viral infection.

Non-viral vectors appear to be a very safe option but are less efficient in terms of how many cells they can enter and express genes in; and how much protein these genes can make. Most non-viral vectors are derived from simple DNA circles (plasmids). These occur naturally in bacteria residing in the nucleus without integration into the chromosomes (and thus without the risk of unmasking a cancer-promoting gene). The excellent safety profile of plasmid DNA has led to its use in approximately 20% of all gene therapy clinical trials.

Need for new diabetes treatment approaches

Despite nearly 90 years experience with conventional insulin therapy, poorly controlled diabetes remains a leading cause of blindness, kidney failure and gangrenous lower limb amputation. The landmark Diabetes Control and Complications Trial in Type 1 diabetes and United Kingdom Prospective Diabetes Study in Type 2 diabetes provided conclusive evidence that these complications could be prevented by tight control of blood glucose levels.

This was, however, counter-balanced by a three-fold increase in significant hypoglycaemia (low glucose reactions), one of the greatest concerns of those living with daily insulin injections. Conventional treatment using insulin injections or pumps has continued to evolve but optimal control continues to be limited by hypoglycaemia.

Transplantation of whole pancreas together with its blood supply or isolated insulin-producing islet cells from a deceased donor offers the potential of a cure, in terms of normalising blood glucose levels without any significant hypoglycaemia. The number of donors is, however, extremely limited and problems can arise if the body starts to reject the new organ.

Patients with a transplant are thus destined to receive life-long immunosuppressive treatment, which increases risk of infection and cancer in addition to other side effects, such as kidney damage.

How could gene therapy be useful for diabetes?

Since everything in life is directed by genes, gene therapy has a huge range of possible applications in diabetes. A few are briefly discussed below:

1.) Immunomodulation
A possible application is prevention of the autoimmune destruction of pancreatic insulin-producing beta-cells (the underlying cause of insulin dependent Type 1 diabetes). Prior to clinically evident Type 1 diabetes, there is a period of silent disease during which the beta-cells are being damaged by the immune system, but diabetes symptoms have not yet occurred.

‘Gene therapy has a huge range of possible applications in diabetes...Gene therapy in mice prone to become diabetic has successfully stopped the immune system from attacking the beta-cells, preventing diabetes.’

Blood tests that check for the presence of antibodies against beta-cells in individuals that are at risk because of a family history of diabetes can tell us which people would benefit from such 'immunomodulation' treatment. Gene therapy in mice prone to become diabetic has successfully stopped the immune system from attacking the beta-cells, preventing diabetes.

The need for life-long immunosuppressant drugs to prevent rejection of 'foreign' pancreas and islet transplants limits this as a realistic treatment option for the majority with diabetes. Immunomodulation using gene therapy may have a useful role in helping the immune system to better tolerate transplanted tissue. Many more studies are needed to fully assess feasibility, safety and effectiveness, however.

2.) Enhanced islet survival and function
A better understanding of the beta-cell destructive process has given scientists insight into a range of very promising candidate genes for increasing cell survival and function after expression in islets. These include specific growth factors, anti-cell-death factors and recently characterised hormones such as glucagon-like peptide-1.

By expressing these genes in the person's own pancreas it might be possible to prevent progression to the need for insulin injections altogether. A similar approach could also prolong the survival of transplanted pancreatic islets. Non-invasive gene delivery to pancreas may be possible using a standard endoscope passed through the stomach enabling injection directly into the pancreatic duct (which drains pancreatic digestive juices into the gut) of conscious or mildly sedated patients.

3.) Insulin gene transfer to non-pancreatic cells
All with Type 1 diabetes and approximately half of those with Type 2 diabetes need insulin to effectively control glucose levels. Long-term restoration of insulin produced by the body following injection of insulin genes into cells which do not usually produce it without the need for pancreas transplantation and avoiding immune rejection is therefore extremely interesting.

The unique features of healthy beta-cells enabling constant precise regulation of the amount of insulin for the appropriate level of blood glucose, might not be easy to transfer to other cell types. Nevertheless, studies in rats and mice transferring insulin genes to muscle, liver and other cells have achieved insulin secretion with much improved diabetic control (**See Fig. 1**).

4.) Insulin sensitisers
Insulin action can be improved by increasing levels of the genes which increase glucose uptake and storage by liver and muscle and this may provide new therapeutic options for Type 2 diabetes, where resistance to the action of insulin is a major contributor to high glucose levels in the blood. For instance, over-expression of the glucose sensor, glucokinase, in the liver has been shown

Continued on page 8

Your questions answered...

Q&A

by Azmina Govindji
Consultant Nutritionist, Registered Dietitian and member of the DRWF Editorial Advisory Board

Pineapple juice and weight gain?

Q As an underweight, (BMI 18.5), I have looked everywhere for some method of increasing weight. Reading a Book by Dr. Andrei Dracea called 'Eat and Heal' I came upon this statement, 'pineapple juice helps persons suffering pancreatic insufficiency gain weight'. As a Type 2 Diabetic this interested me, particularly as the only time I put on weight was when on holiday in Sri Lanka some years ago, where pineapples were available every where. The problem is, would the sugar content in juice available over here be too high? Would you please ask your nutritional experts for their comments?

A If you're concerned about being underweight, you should consult your GP so he can check for any underlying conditions preventing you from gaining weight. To gain weight, you need to eat more calories than you use up in daily activities. It's not enough just to have occasional extra snacks, and having diabetes means that the snacks and meals you choose need to be in line with healthy eating and good blood glucose control.

If you reach for chocolates, sweets and fizzy drinks, not only will this hamper your diabetes, it also makes you more likely to gain fat instead of lean muscle mass. Here are five tips to help you gain weight in a healthy way:

1. Aim for three meals and three snacks a day.

2. Remember the general principles of a healthy diet for diabetes. Choose wholegrain starchy foods and base meals on carbohydrates such as wholegrain bread, pasta, brown rice, beans and lentils.

3. Drinking fruit juices such as pineapple juice, especially in between meals, will make your blood sugar go up. So have a small glass of fruit juice but try to limit the amounts, say to once a day. Instead, focus on a variety of fruit and vegetables. They can be fresh, frozen or canned.

4. Include protein foods at each meal. This could include lean meat, fish, eggs, lower fat dairy products, beans and lentils or nuts.

5. Try fortified milk powders which you can get from the supermarket or the pharmacy. You could use these in hot drinks to add calories, protein and nutrients.

Fructose use by people with diabetes

Q I am writing to make some enquiries concerning the use of sweetener and Fructose by people with diabetes. The question has been raised by the increased use of these substances and the changes in description on some diabetic chocolate bars. The words 'sugar free' are now replaced with 'sweetened by fructose'. One diabetic I know claims that the smallest quantity of this substance immediately sends his sugar reading too high. I read recently of the danger of drinking pure fruit juice with or without fruit pieces as it sends a directly high volume of natural sugar into the bloodstream. I would appreciate your views on this matter.

A Firstly, make sure that you seek guidance from your own registered dietitian. Well-meaning friends and articles on the Internet can be helpful but also sometimes can be confusing, so it's best to keep to the advice that you can trust. In terms of glycaemic index, fructose does have a lower glycaemic index than ordinary white sugar or sucrose. This is why you will sometimes find fructose in special diabetic foods. Remember firstly that people with diabetes do not need special diabetic products. It's fine to have small amounts of ordinary chocolate at the end of the meal, as part of a healthy diet.

Secondly, fructose is a type of sugar so a product that contains fructose is not strictly sugar free. Fructose is naturally found in fruit but when it is used as a sweetener, it really has no significant advantage over sucrose. If a food is sweetened with fructose, it doesn't mean it's any lower in calories than an ordinary food and your blood sugar will still be affected by the fructose. When fructose is taken in as part of a liquid, as in fruit juice, your blood sugar will rise quicker than if it is naturally intact in a piece of fresh fruit. So, it's best to eat a variety of fresh fruit and vegetables rather than have a lot of fruit juice, even if it is unsweetened fruit juice.

IMPORTANT:

Please be aware that these questions are personal answers to individual's medical queries and so may not be suitable advice for everyone, dependent upon your medical history. These questions are in no way meant to compensate for the advice of your own doctor. If you have an urgent medical query see your doctor or diabetes nurse immediately.

If you are visually impaired we can supply a copy of the Diabetes Wellness News in alternative formats. Please call 02392 636132 to discuss your requirements.

Continued from page 1
to normalise fasting blood glucose in rodent insulin-deficient and insulin-resistant diabetes.

5.) Anti-obesity gene therapy
Better understanding of the factors affecting appetite and weight, has helped to uncover a wide range of novel targets for gene therapy. This offers the potential of weight loss in obesity with enhanced insulin sensitivity and improved glucose tolerance in Type 2 diabetes. Decreased food intake and a reduction in body weight with lower insulin levels and normal glucose levels have been achieved in mice following gene transfer of the hormone, leptin, to muscle.

6.) Gene therapy targeted at diabetic complications
Finally, there are many potential gene therapy applications targeted at the long-term complications of diabetes. Examples include therapy that promotes the health and growth of blood vessels for diabetes-induced vascular disease. Small scale clinical trials have recently been undertaken in which 'VEGF', a factor which promotes blood vessel health and growth, was injected into the muscle where disease had caused severe damage to the blood supply of the legs. This resulted in possible benefits without any adverse effects.

Other applications are gene therapy approaches for diabetic eye disease directly targeted to the eye and gene therapy which uses 'erythropoietin' DNA. This latter hormone can be deficient in diabetic patients with kidney disease causing red blood cell numbers to decrease (anaemia). Similarly, gene transfer into the muscles of factors that promote the health of nerves could play a major role in the prevention of diabetic foot.

'Although real clinical breakthroughs in diabetic gene therapy approaches have yet to be realised, it remains likely that one or more of the pioneering approaches currently being explored will enter trials within the next few years.'

Concluding comments and the future

Following early enthusiasm, gene therapy has often been dismissed in favour of newer innovations such as stem cell transplantation. Incremental progress has continued, however, with real progress in the development of gene delivery without the limiting toxicity of early-generation viral vectors.

Although real clinical breakthroughs in diabetic gene therapy approaches have yet to be realised, it remains likely that one or more of the pioneering approaches currently being explored will enter trials within the next few years.

Tale end

Winter blues

It must be a bad winter. Earthlings have a condition called SAD which they treat with light therapy.

MISSION STATEMENT

The Diabetes Wellness Network™ was founded because people with diabetes have to make decisions about their general health as well as their diabetes. The Diabetes Wellness Network™ aims to help you deal with these problems, whilst bearing in mind your diabetic condition. With the Diabetes Wellness News, we work towards educating, informing and reminding you of the best and healthiest choices to make. The Diabetes Wellness News is a digest of magazines, newspapers, books and scientific journals – bringing you, as well, first-class articles from respected diabetes and other professionals. It is not, however, a substitute for medical care from a physician or health care team.

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