Number of US diabetics rises to approximately 26 million

"These distressing numbers show how important it is to prevent Type 2 diabetes and to help those who have diabetes manage the disease to prevent serious complications such as kidney failure and blindness."

The Centre for Disease Control and Prevention has announced new estimates of the number of American's with diabetes and prediabetes.

According to the recently released National Diabetes Fact Sheet 2011, approximately 26 million people in the USA have diabetes and approximately 79 million have prediabetes.

Prediabetes is a condition where blood sugar levels are raised, but are not high enough to be diagnosed as diabetes. Prediabetes increases the risk of Type 2 diabetes, heart disease and stroke. A total of 35% of US adults are thought to be affected by prediabetes.

"These distressing numbers show how important it is to prevent Type 2 diabetes and to help those who have diabetes manage the disease to prevent serious complications such as kidney failure and blindness," explained Ann Albright, Centers for Disease Control and Prevention, Division of Diabetes Translation, (GA, USA). "We know that a structured lifestyle program that includes losing weight and increasing physical activity can prevent or delay Type 2 diabetes."

In 2008 the Centre for Disease Control and Prevention estimated that 23.6 million people in America had diabetes and another 57 million US adults had prediabetes. The rise in these numbers by 2011 can be explained by several factors.

First, more people are developing diabetes. Second, there is an increase in life expectancy for diabetes patients. This is thought to be a result of improved management of the disease, leading to a reduction in complications, such as amputation, cardiovascular disease and kidney failure.

The third factor to be considered is the new Hemoglobin A1c diagnostic test. The test measures blood glucose over a 2–3 month period and may have lead to an increase in the number of diabetic patients diagnosed. Owing to this additional test, it must be noted that the 2008 and 2011 estimates cannot be compared directly.

The fact sheet was prepared in collaboration with a number of agencies within the US Department of Health and Human Services, other federal agencies, the American Association of Diabetes Educators, the American Diabetes Association and the Juvenile Diabetes Research Foundation International. A number of sources were used to draw up the estimates used on the new fact sheet, including Centre for Disease Control and Prevention surveys, the Indian Health Service National Patient Information Reporting System, the US Renal Data System of the National Institutes of Health, the US Census Bureau and other published studies.

Sources: CDC Online Newsroom: CDC Division of News and Electronic Media: www.cdc.gov/media/releases/2011/p0126_diabetes; www.cdc.gov/diabetes/pubs/factsheet11

"...26 million people in the US have diabetes and approximately 79 million have prediabetes."

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New discovery may lead to a cure for insulin-dependent diabetes

New findings from the University of Texas Southwestern Medical Center, (TX, USA), suggest that simply eliminating the actions of one hormone could convert Type 1 diabetes into an asymptomatic disorder, negating the need for insulin injection.

Roger Unger, Professor of Internal Medicine at UT Southwestern, and colleagues had previously demonstrated that the benefits of insulin stem from its suppression of glucagon.

In the present study the group genetically altered mice so they did not produce glucagon receptors, in an attempt to return their glucose tolerance to normal. They then monitored the response in these mice to an oral glucose test that measures glucose metabolism following a meal.

Interestingly they discovered that both mice with normal insulin production and mice with impaired insulin production (achieved by destroying insulin producing β-cells) responded normally to the glucose tolerance test.

> "...simply eliminating the actions of one hormone could convert Type 1 diabetes into an asymptomatic disorder..."

Commenting on the results, Unger explains that it appears that "if there is no glucagon, it doesn't matter if you don't have insulin." However, he provides a warning that, "this does not mean insulin is unimportant. It is essential for normal growth and development from neonatal to adulthood. But in adulthood, at least with respect to glucose metabolism, the role of insulin is to control glucagon."

Dr Unger concludes that anything resulting in a reduced need for insulin injection is a positive and that any future treatment resulting from this discovery could "perhaps be considered very close to a 'cure'," for Type 1 diabetes.

> "...anything resulting in a reduced need for insulin injection is a positive..."

Looking to the future Young Lee, Assistant Professor of Internal Medicine at UT Soutwestern, hopes that further studies will uncover the mechanism behind the results discovered in mice; "if we can find a way to block the actions of glucagon in humans, then maybe we can minimize the need for insulin therapy."

Source: Lee Y, Wang MY, Du XQ, Charron MJ, Unger RH: Glucagon receptor knockout prevents insulin-deficient Type 1 diabetes in mice. *Diabetes* 60(2), 391–397 (2010).

Researchers discover a new mechanism behind blood sugar level control

Medical scientists at the University of Leicester, UK, have identified the role of a new protein in controlling blood sugar levels.

Andrew Tobin, Professor of Cell Biology at the University of Leicester and a Wellcome Trust Senior Research Fellow, and his group, focus their research on the mechanisms employed by the body to control blood sugar levels after eating.

In their present study they produced a knock-in mouse strain that expressed a phosphorylation-deficient mutant of the M_3-muscarinic receptor. This mouse strain was then used to investigate the role of M_3-muscarinic receptor phosphorylation in the regulation of insulin secretion from pancreatic islet cells.

The group found that their knock-in mice had impaired glucose tolerance as well as impaired insulin secretion. This indicated that the M_3-muscarinic receptors expressed on pancreatic islet cells are involved in regulating glucose homeostasis. Further investigations demonstrated that the mechanism is dependent on the recruitment of β-arrestin to phosphorylated M3-muscarinic receptors and subsequent activation of downstream protein kinase D1. They found that activation of protein kinase D1 was essential for muscarinic-receptor-augmentation of insulin release from islet cells.

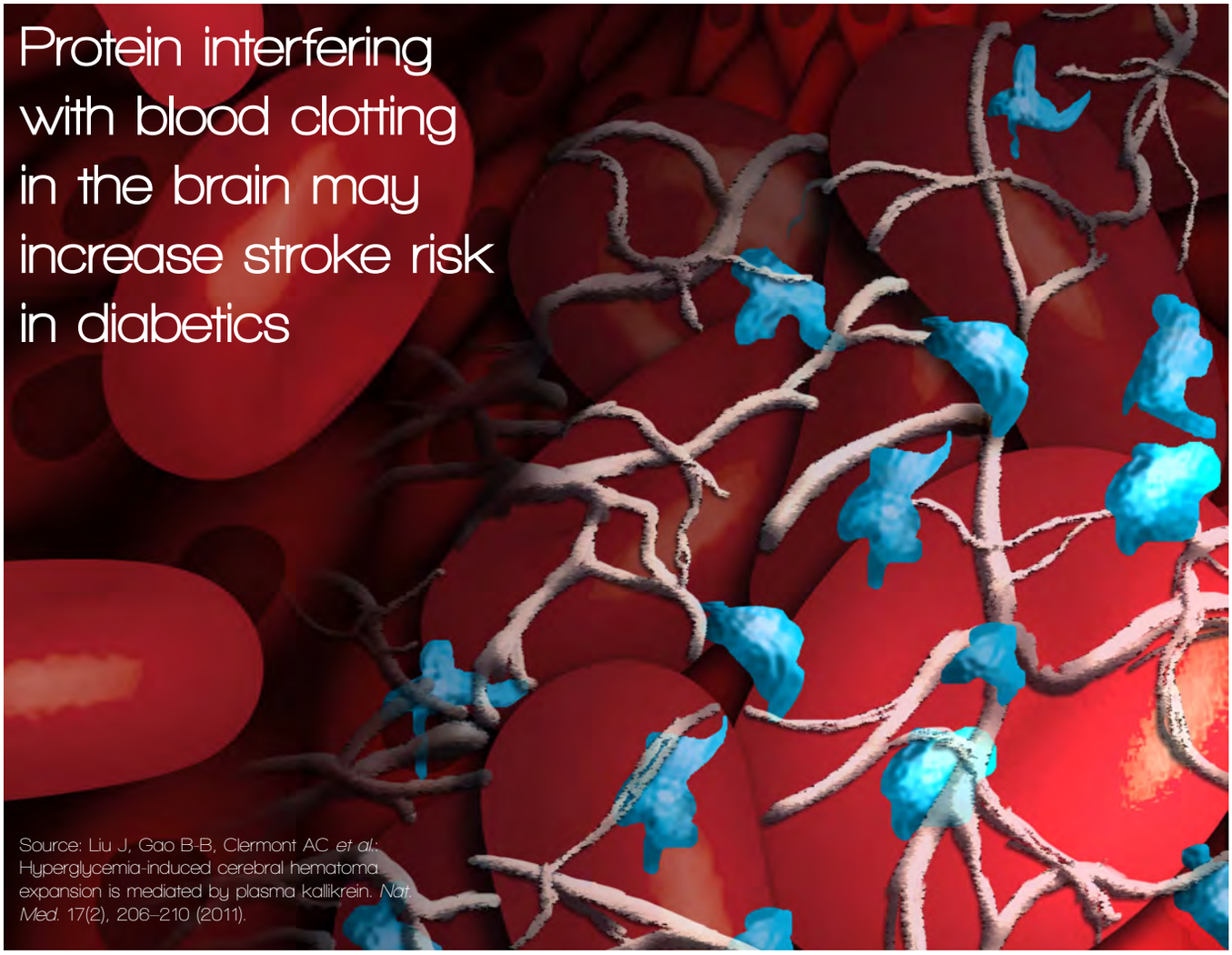
The phosphorylation-deficient M_3-muscarinic receptor, present in the knock-in mice, showed reduced interaction with protein kinase D1. This reduced interaction correlated with the inability of these mice to regulate insulin release and glucose homeostasis.

The group conclude that their results present evidence for a unique mechanism of muscarinic-mediated insulin release and glucose homeostasis.

Tobin adds that while the rise in sugar levels observed is similar to that in diabetes, "we are of course testing if the mechanism of controlling sugar levels we have discovered is one of the mechanisms disrupted in diabetes. If this were the case then our studies would have important implications in diabetes."

Source: Kong KC, Butcher AJ, McWilliams P *et al.*: M3-muscarinic receptor promotes insulin release via receptor phosphorylation/arrestin-dependent activation of protein kinase D1. *PNAS* 107(49), 21181–21186 (2010).

Protein interfering with blood clotting in the brain may increase stroke risk in diabetics



Source: Liu J, Gao B-B, Clermont AC *et al.*: Hyperglycemia-induced cerebral hematoma expansion is mediated by plasma kallikrein. *Nat. Med.* 17(2), 206–210 (2011).

A key protein has been identified that may increase bleeding during hemorrhagic stroke.

High blood glucose levels, as a result of diabetes and hyperglycemia, are associated with increased bleeding during hemorrhagic stroke.

Researchers at the Joslin Diabetes Center, (MA, USA), have found that a protein, known as plasma kallikrein, effects blood clotting in the brain following blood vessel injury with diabetes. They have identified the mechanism by which bleeding is increased. Plasma kallikrein was found to block the activation of platelets in areas surrounding damaged blood vessels.

Experiments were carried out on diabetic rats and nondiabetic rats. When blood was injected into the rat's brains, the diabetic rats bleed over a much greater area. When the diabetic animals were treated with a molecule that inhibits its plasma kallikrein function, brain damage resulting from blood injections was increased. When the animals were injected with pure plasma kallikrein, bleeding increased rapidly in the diabetic animals, although little effect was seen in the nondiabetic controls.

> "High blood glucose levels ... are associated with increased bleeding during hemorrhagic stroke."

When researchers normalized blood sugar levels in diabetic rats the effect of plasma kallikrein was blocked. Therefore, it is thought that high blood sugar levels in the brain at the time of hemorrhage is likely to lead to increased bleeding, rather than diabetes itself.

"Given the prevalence of strokes and the damage they inflict, these findings are exciting because they suggest the possibility that rapid control of blood sugar levels may provide an opportunity to reduce intracerebral hemorrhage, which is a clinical situation that has very limited treatment options," explains Edward Feener from Joslin Diabetes Center (MA, USA), who worked on the study. "This work could have broad implications since approximately half of patients with acute hemorrhagic stroke have hyperglycemia, whether or not they have pre-existing diabetes."

In future drugs could be developed that target plasma kallikrein, potentially protecting people with diabetes against their high risk of stroke.

Study to be carried out into why some diabetics escape complications associated with the disease

The PROLONG study will investigate the differences between diabetics who have been complication-free for 30 years or more and those who develop diabetes associated conditions, such as nephropathy and heart disease.

> **"**...there are a significant proportion of diabetic individuals who do not develop any severe complications associated with their diabetes.**"**

A new study looking at why some diabetic individuals never develop severe complications associated with the disease is to be carried out in Sweden. The Protective Genes in Diabetes and Longevity (PROLONG) study will compare a cohort of individuals who have had diabetes for over 30 years without complications with a group who developed severe complications from diabetes after having the condition for less that 15 years. It is hoped that information gleaned from these 'diabetic veterans' will help to inform management and prevention of severe complications associated with diabetes.

The PROLONG study which will act as a pilot study is to be carried out in Skåne, Sweden. Valeriya Lyssenko and Peter Nilsson (Lund University Diabetes Centre, Sweden), who are both working on the study, note that the long-term plan will be to roll out the study to all hospitals in Sweden. There are severe complications associated with diabetes, including nephropathy, retinopathy, heart attacks and stroke. It is estimated that 70% of diabetics will develop some form of nephropathy and/or retinopathy in their lifetime and the risk of dying from heart disease is two- to three- times higher among the diabetic population as compared with the nondiabetic population. The mechanisms associated with the increased risks of these complications in diabetes are not completely understood and the damage to blood vessels associated with long-term diabetes can neither be treated nor prevented. Despite this, there are a significant proportion of diabetic individuals who do not develop any severe complications associated with their diabetes. These 'resistant' individuals are of great interest to Lyssenko and his team as he notes "The majority of diabetics will over time develop severe or fatal complications, but 10–15% never do. They are the ones we are interested in the PROLONG study."

"If we can identify factors protecting these veterans from devastating complications, then it might be possible to develop drugs that can do the same thing" Lyssenko explains.

Source: Lund University press release, via AlphaGalileo: www.alphagalileo.org

About the News

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