Diabetes: Fact Sheet

Insulin is a pancreatic peptidic hormone that regulates sugar metabolism. Diabetes mellitus (DM) is a chronic disease that occurs when the pancreas does not produce enough insulin, or alternatively, when the body cannot effectively use the insulin it produces. Hyperglycemia, or raised blood sugar, is a common condition of uncontrolled diabetes. Over time, it leads to serious damage to many of the body's systems, especially the nerves and blood vessels. The market for diabetes treatment has grown by a compound average rate of almost 20% over the last decade, from almost $4 billion in 1995 to more than $17 billion in 2005.[1] Overall, anti-diabetic drug sales are expected to increase to $22 billion by 2012 as the addressable patient population continues to increase.[1] The World Health Organization estimates that more than 180 million people worldwide have diabetes and this number is likely to more than double to approximately 370 million by 2030.[2]

Type 1 diabetes, previously known as juvenile-onset diabetes or insulin-dependent diabetes, is characterized by a lack of insulin production. Without daily administration of insulin, Type 1 diabetes is rapidly fatal. Type 2 diabetes, previously known as adult-onset diabetes or non-insulin dependent diabetes, results from the body's ineffective use of insulin. Type 2 diabetes comprises 90% of people with DM around the world, and is largely the result of excess body weight and physical inactivity. A third type of diabetes, gestational diabetes mellitus (GDM), develops during some cases of pregnancy but usually disappears after pregnancy.

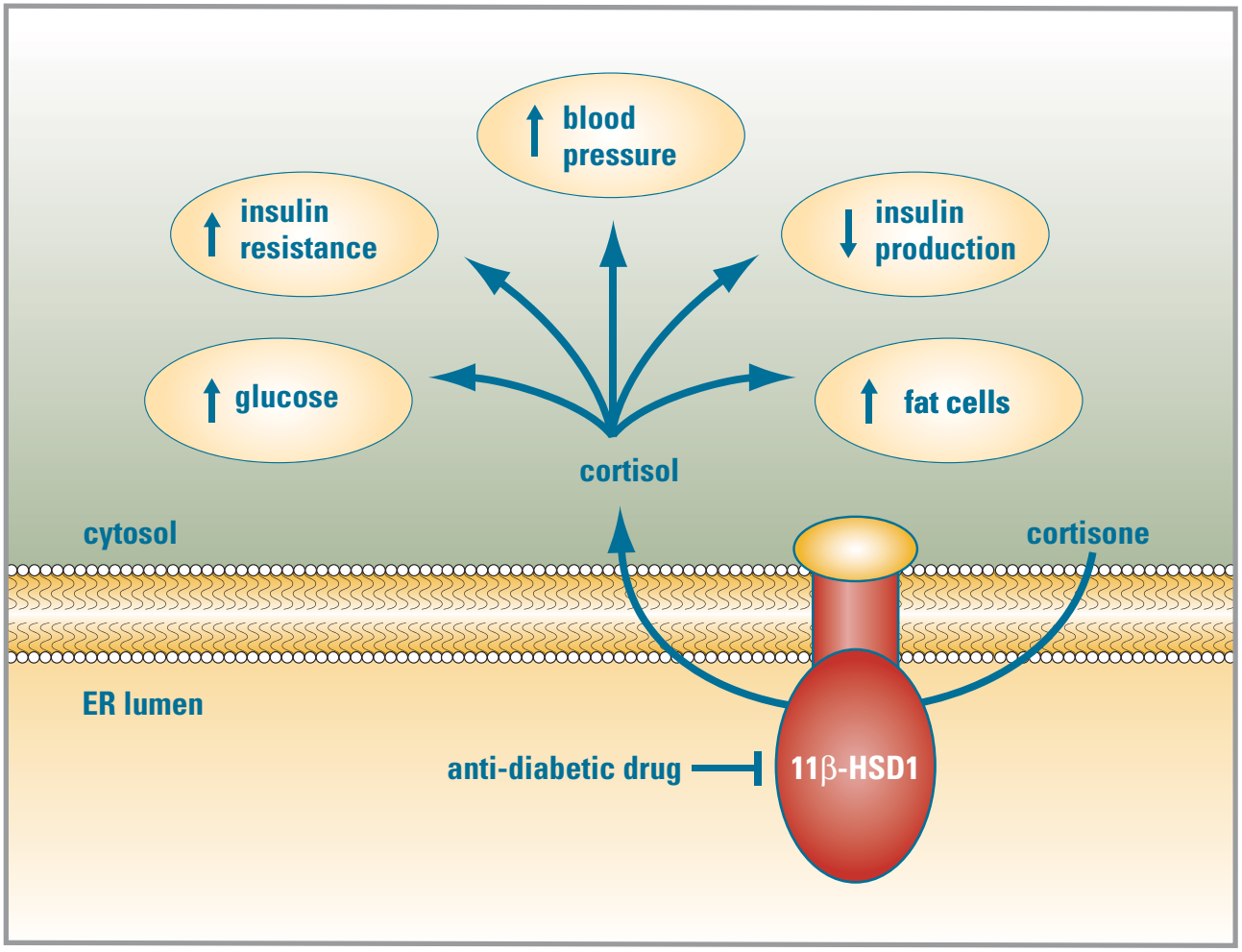
People with Type 1 diabetes require daily injections of insulin to survive. People with Type 2 diabetes can sometimes manage their condition with lifestyle measures alone. However, oral drugs are often required, and sometimes insulin, in order to achieve good metabolic control. A number of drug therapies are available for treating diabetes. They are given either alone or as combinations with or without insulin injections. These medications generally fall into the categories of:

Drug Class	Mode of Action	Examples
Sulfonylureas	Stimulating beta cells to increase insulin production	glipizide, glyburide
Meglitinides	Also known as postprandial glucose (PPG) regulators, these compounds act by stimulating insulin secretion from the pancreas	nateglinide, repaglinide
Biguanides	Inhibiting hepatic glucose production and increasing the sensitivity of peripheral tissues to insulin	metformin
Thiazolidinediones	Increasing peripheral glucose utilization in skeletal muscle and adipose tissue, reducing hepatic glucose output, increasing fatty acid uptake and reducing lipolysis in adipose cells	pioglitazone, rosiglitazone
Alpha-glucosidase inhibitors	Slowing enzymatic degradation of complex carbohydrates and hence reducing absorption of glucose	acarbose, miglitol
Dipeptidyl-peptidase-4 (DPP-4) inhibitors	Blocking an enzyme called DPP4 which breaks down peptides that boost the release of insulin after blood sugar rises, such as after a meal	saxagliptin, sitagliptin

Existing therapies have also been associated with various drawbacks and side effects such as weight gain, GI side effects, increased risk of hypoglycemia, liver toxicity and high cost.

Hydroxysteroid Dehydrogenase Inhibitors

Glucocorticoids are hormones found naturally in the body that help regulate carbohydrate, fat, and protein metabolism. The primary glucocorticoid in man, cortisol, opposes the secretion and action of insulin in multiple tissue types and is thought to play a central role in the development and progression of diabetes. The 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) enzyme regulates glucocorticoid activity and catalyzes the conversion of inactive cortisone to active cortisol in active target tissues. Therefore, inhibition of 11β-HSD1 activity offers the potential of a novel therapeutic for diabetes and obesity by restoring the glucose-lowering action of insulin.



References

1 R&D Directions, Volume 12, Number 9, Page 52, October 2006

2 World Health Organization Fact Sheet No. 312, September 2006