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VEPACHEDU EDUCATIONAL FOUNDATION

The Andhra Journal of Industrial News

IP and Industry News

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Issue 120

History of Insulin

Insulin is a hormone made by the pancreas to control blood glucose levels. Insulin is the “key,” which unlocks the cell to allow sugar to enter the cell and be used for energy. When blood glucose levels fall below a certain level, the body begins to use stored sugar as an energy source through [glycogenolysis](#), which breaks down the glycogen stored in the liver and muscles into glucose, which can then be utilized as an energy source. If pancreas does not produce enough insulin (Type I) or the cells are resistant to the effects of insulin (Type II), diabetes or hyperglycemia (high blood sugar) results, which can cause long-term complications. Insulin is a naturally occurring and very (about one billion years) old protein. Diabetes is also a very old disease that afflicts humans and animals. Diabetes affects more than 13 million in Russia (~8%), 25 million in the US (~8%), 90 million in China (6%), and 61 million in India (~4%)¹. New figures indicate that the number of people living with diabetes is expected to rise from 366 million this year to 552 million by 2030².

The earliest description of diabetes appeared in a collection of medical texts in India and Egypt. Ants

¹https://images.search.yahoo.com/images/view;_ylt=AwrB8pgVDA9TnSwAZWGIJbkF;_ylu=X3oDMTIzcG5rY2llBHNIYwNzcgRzbGsDaW1nBG9pZAM0YmNhMmZiZjQwOGQzOTU3ZWQ3OWFjYzIxMWE0ZWUxOQRncG9zAzI0BG10A2Jpbmc-?back=https%3A%2F%2Fimages.search.yahoo.com%2Fsearch%2Fimages%3F_adv_prop%3Dimage%26va%3Ddiabetes%2Bindia%26fr%3Dmcsaoffblock%26tab%3Dorganic%26ri%3D24&w=960&h=720&imgurl=www.sanofidiabetes.in%2Fimages%2Fhcp%2FEpidemiology3.jpg&rurl=http%3A%2F%2Fwww.sanofidiabetes.in%2FEpidemiology.aspx&size=80.9KB&name=Epidemiology+and+Burden+of+%3Cb%3EDiabetes%3C%2Fb%3E&p=diabetes+india&oid=4bca2fbf408d3957ed79acc211a4ee19&fr2=&fr=mcsaoffblock&tt=Epidemiology+and+Burden+of+%3Cb%3EDiabetes%3C%2Fb%3E&b=0&ni=21&no=24&ts=&tab=organic&sigr=11ea6lsr7&sigb=13hsdk927&sigi=11id8oq1s&sigt=11af4q4bi&sign=11af4q4bi&.crumb=/U0Q7h.267x&fr=mcsaoffblock
² <http://timesofindia.indiatimes.com/india/Indias-diabetes-burden-to-cross-100-million-by-2030/articleshow/11101062.cms>

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were diagnosing diabetes in humans thousands of years ago, according to ancient Hindu writings. Diabetes mellitus and its medicinal remedies were described in ancient India, Egypt and China. As early as the 16th century B.C. people had been interested in this terrible affliction that produced terrible thirst, nearly continual urination, severe weight loss and ultimately, a prolonged and painful death. In fact, the use of exercise in the treatment of diabetes was prescribed as early as 450 BC by the Indian physician Sushruta. These early records describe people with a mysterious and deadly disease that caused intense thirst, enormous urine output, and wasting away of the body. An early clue was the attraction of ants and flies to the urine of the victims³.

For thousands of years, no one knew how to live with, let alone correct, diabetes. Children with the disease died quickly, often within days of onset, and older folks struggled with devastating complications. Aretaeus of Cappadocia, a Greek physician, (129–199 AD) introduced the term “diabetes” from the Greek word “siphon” as he noted that diabetes causes constant flow of urine. Before the availability of insulin, the life expectancy of children with diabetes mellitus was short and the prognosis for the adult onset diabetes was very poor. Controlling high blood sugar helps prevent kidney damage, blindness, nerve problems, loss of limbs, and sexual function problems. Proper control of diabetes may also lessen your risk of a heart attack or stroke. Man-made insulin product is the same as human insulin. It replaces the insulin that the body would normally make. This medication is usually used in combination with a medium- or long-acting insulin product. This medication may also be used alone or with other oral diabetes drugs (such as metformin).

Insulin is used with a proper diet and exercise program to control high blood glucose in people with diabetes. Various types of insulin are used to treat diabetes and include rapid, short, intermediate, and long-acting insulins. Insulin can be given by a syringe, injection pen, or an insulin pump that delivers a continuous flow of insulin. However, no civil liberties or anti-patent organizations made an effort to bring insulin to poor diabetics of the world for millions of years since the beginning of the human race.

Banting, Macleod, Best and Collip invented the process for insulin in 1922 which marked a major breakthrough in medicine and therapy in patients with diabetes. Frederick Banting, an orthopedic surgeon,

³ http://www.diabetesindia.com/diabetes/history_diabetes2.htm http://www.diabetesindia.com/diabetes/history_susruta.htm

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had the idea of isolating pancreatic islet extracts by ligating the pancreatic duct of dogs, keeping them alive until the acini degenerated, leaving the islets for isolation. He approached John Macleod, professor of physiology and department head at the University of Toronto, for laboratory space. Macleod granted him laboratory space, ten dogs for his experiments, a student research assistant Charles Best, and provided supervision and guidance. The experiments began on May 17, 1921. Soon, biochemist J.B. Collip joined the group and helped purify the isletin for human use. The first injection of the pancreatic extract to a 14-year-old boy by Banting and Best on January 11, 1922. In 1923, Banting, Best, and Macleod were awarded the Nobel Prize. Eli Lilly began producing insulin from animal pancreas. In 1923, August Krogh, from the University of Copenhagen, obtained authorization from the University of Toronto and soon Nordisk Insulin Laboratory began insulin production in Scandinavia.

In the 1930s, Hagedorn, a chemist in Denmark, prolonged the action of insulin by adding protamine, while Scott and Fisher, in Toronto, prolonged insulin action further by adding zinc. These discoveries led to the introduction of longer-acting animal insulins in the market. In 1982, the first insulin utilizing rDNA technology, Humulin[®] R (rapid) and N (NPH, intermediate-acting), were marketed by Genentech and Lilly. Lispro was the first short-acting insulin analog approved in 1996, followed by aspart in 2000, and glulisine in 2004. Currently, there are two basal insulin analogs in the market, glargine, approved in 2000 and detemir, approved in 2005.

Delivering insulin through other than a needle, such as insulin in a pill would be better, but is not feasible because insulin is a peptide and would be digested in the stomach. The idea of inhaling insulin has been around for decades where insulin particles are delivered through an inhaler into the lungs and the bloodstream through tiny blood vessels. After more than 80 years of history the American and European Drug Agencies (FDA and EMEA) approved the first pulmonary delivered version of insulin Exubera, only to be rejected by the market and healthcare industry in 2007, shocking pharmaceutical companies and venture capitalists. As a result, Eli Lilly's AIR insulin was also suspended. For many patients, avoiding the need for SC injections is attractive; however, as long as no clear 'advantage' can be demonstrated, reimbursement will be difficult to achieve and the drug is bound to fail in delivering dollars for shareholders. Exubera and AIR insulin had not offered profound advantages in terms of pharmacokinetic (PK) and pharmacodynamic (PD) properties in comparison with subcutaneously (SC) applied regular human insulin (RHI) and rapid-acting insulin analogues. However, one man still standing,

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despite risks, is Al Mann, who was able to manage a number of challenges during the clinical development process successfully. The FDA, after three years of additional studies approved Afrezza, an insulin powder, comes in a single-use cartridge and is designed to be inhaled at the start of a meal. It is success, of course, depends on healthcare industry.

Insulin therapy witnessed tremendous progress in the past century, from the initial crude animal insulin extracts to novel human insulin analogues. Hopefully, the continued development of improved insulin formulations with superior pharmacokinetics and pharmacodynamics will enhance glucose control, and represents important clinical advances in the treatment of both type 1 and type 2 diabetes⁴.

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Source: The primary sources cited above, New York Times (NYT), Washington Post (WP), Mercury News, Bayarea.com, Chicago Tribune, USA Today, Intellihealthnews, Deccan Chronicle (DC), the Hindu, Hindustan Times, Times of India, AP, Reuters, AFP, womenfitness.net, about.com, mondaq.com, etc.

Om! Asatoma Sadgamaya, Tamasoma Jyotirgamaya, Mrityorma Amritamgamaya, Om Shantih, Shantih, Shantih!
(Aum! Lead the world from wrong path to the right path, from ignorance to knowledge, from mortality to immortality, and peace!)

⁴ Quianzon et al., History of Insulin, J Community Hosp Intern Med Perspect. 2012; 2(2): Published online Jul 16, 2012, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3714061/#CIT0017>,

Polin, Insulin: Its History and Future, <http://www.diabetictlifestyle.com/blood-glucose/insulin-its-history-future>

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