From the Pages of History

The Discovery of Insulin

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The Nobel Prize money is obtained from the fortune of Alfred Nobel for his invention of dynamite. It was thought that the Nobel Prize was instituted because of an earlier publication of an obituary 'The Merchant Of Death Is Dead' in a newspaper which confused his brother's death with his own. Whatever be the trigger for establishing the Nobel Prize, winning the Nobel Prize signifies achieving excellence in one's field.However, even the Nobel Prize has its share of controversies. In 1923, Frederick Grant Banting (1891-1941) and John James Richard Macleod (1876-1935)won the Nobel Prize for physiology or medicine for the discovery of insulin and this has not been free from controversy since then. Frederick G. Banting and John Macleod won the Nobel Prize in Physiology or Medicine in 1923 "for the discovery of insulin."

Introduction

Oskar Minkowski (1858-1931) in 1889, discovered incidentally that removing the pancreas in dogs caused a serious form of diabetes[1]. A medical student Paul Langerhans (1847-1888) discovered the islet cells in the pancreas, the secretion of which was thought to be involved in diabetes[2]. But as for the discovery of the active component, numerous scientists followed the work of Minkowski but were unsuccessful in their their attempt to extract it. Between 1914 and 1916 it was the Romanian physiologist Nicolas C Paulescu who first extracted a pancreatic anti diabetic agent that healed dogs but these experiments would be overlooked in favour of work by other scientists[3]. In 1922, the Lancet expounded that a simpler method of measuring blood sugar might have led to earlier discovery of insulin ; 25-50 ml of blood and 3 hours were required to test sugars then[4].

Fred Banting started his study of medicine in 1912 at the University of Toronto. He wanted to become a surgeon at the Toronto Hospital but became a demonstrator at the University of Ontario. He read an article on 'The relation of the Islets of Langerhans to diabetes' while preparing a student lecture on carbohydrate metabolism and he proposed in his notes:

'Diabetus:

Ligate pancreatic ducts of dog. Keeping dogs alive until acini degenerate leaving islets.

Try to isolate the internal secretion of these to relieve glycosurea.'[4]

As the University of Toronto had good research facilities under John James Richard Macleod ,a famous physiologist and expert in carbohydrate metabolism , Banting was referred to him . During their first meeting on 7th November, 1920, Macleod was unreceptive to Banting's idea and suspicious of his abilities as a researcher . Macleod wrote, " I found that Dr.Banting had only a superficial textbook knowledge of the work that had been done on the effects of pancreatic extracts in diabetes and that he had very little practical familiarity with the methods by which such a problem could be investigated in the laboratory. "For his part Banting wrote ,"Macleod put me off saying that many men had worked for years in well equipped laboratories and had not even proved that there an internal secretion of the pancreas[4]. "However in the end , Macleod said that even negative results would be of great value. In April 1921 ,Banting was given a small unused room in the department of physiology. Macleod had insisted on measuring the blood sugar as the experiment 's end point for which Banting required an assistant. Moreover Banting had never done a pancreatectomy and was shown how to do so by Macleod on May 16.Macleod's students Charles Best and Clark Noble were offered the chance to earn money by helping Banting. Best won the coin toss and was the first to work with Banting[4].

In June 1921 ,Macleod went to Scotland on a holiday, thereby giving rise to the controversy of how much advice Banting obtained from him. Banting pressed on with great determination and on 30thJuly, he and Best injected a pancreatic extract into a depancreatized dog and observed a sharp fall in its blood sugar .In their efforts to make the pancreatic extracts work consistently Banting and Best were joined by James Bertram Collip (1892-1965), an associate professor of biochemistry. Banting 's presentation of his and Best's results in December however met with substantial criticism[1-3].

Banting, right, and Best, left, with one of the diabetic dogs used in experiments with insulin.
Credits: University of Toronto Archives

On 11th January 1922, Banting and Best made an extract from the pancreas which was injected into a 14 year old diabetic boy, Leonard Thompson. This however had disappointing results. However Collip worked furiously to modify the extract by removing toxic contaminants from it and the experiment was resumed on January 23rd with spectacular success.

When asked by Banting for details of the effective extract , Collip would not tell him. This resulted in a fight in which Collip was grabbed by the collar by Banting . On 22nd March 1922, after peace had been brokered, the group published an initial report of its results on Thompson and other patients in the Candian Medical Association Journal. On May 2nd 1922 ,on presentation of the results of the clinical trial by Macleod to the Association of American Physicians ,he and his associates were given a standing vote of appreciation .

In 1923, Banting and Macleod were awarded the Noble Prize. Banting was angry at Macleod being nominated along with him . He was persuaded to accept the Nobel Prize by the Chairman of Insulin Committee since this was the first time a Canadian had been awarded the Nobel Prize. Banting shared his money with Best as did Macleod with Collip.

That the treatment of diabetes was revolutionised overnight was what was popularly believed after the discovery of insulin. However a lot of doctors were scared to use it and the editor of the Medical Journal of Australia called insulin an unproven therapy which was dangerous to patients. Insulin was used only as a last resort as not only were the most visible effects were seen in the previously fatal diabetic ketoacidosis and coma, but it was also very expensive. Long acting insulin was introduced in 1936-37. But in the next two decades,doctors found that while insulin saved the lives of juvenile diabetics , they were however developing complications such as loss of vision and kidney failure. It was not until 1993 that the results of the American Diabetes Control and Complications Trial (DCCT) were published which showed that good glycemic control could prevent or delay the onset of complications.

Connaught Laboratories, later called Eli Lilly and Co., took over manufacture of insulin in Toronto .Insulin from cattle and pigs was used for many years to treat diabetes .The first genetically engineered synthetic human insulin was produced in 1978 . The technique used *E.coli* bacteria to produce insulin. So now what's next? Oral insulin? Scientists are working hard on it!

References

1) "The Discovery of Insulin". Nobelprize.org. Nobel Media AB 2014. Web. 12 Sep 2016. <http://www.nobelprize.org/educational/medicine/insulin/discovery-insulin.html>

2) The Discovery Of Insulin - How Was Insulin Discovered? www.medicalnewstoday.com/info/diabetes/discoveryofinsulin.php

3) The Discovery of Insulin - The Canadian Encyclopedia www.thecanadianencyclopedia.ca/en/article/the-discovery-of-insulin/

4) Thompson G:Nobel Prizes that changed Medicine 2012, Imperial college Press,London

Answer to : **Diagnose the Condition**

ECG showing narrow complex tachycardia. It is regular with Atrial and ventricular rate of 160 per minute.Inverted P wave seen after the QRS complex. The RP interval is shorter than the PR interval. So a short RP tachycardia. The RP interval is aroung 70 to 80 ms, suggestive of AVNRT (AV nodal re-entrant tachycardia). The SVT reverted with I.V Adenosine.

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