JJRM website – draft Biographical Chapters

**Early Life [1876-93]**

John James Rickard Macleod was born on 6th September 1876 in the manse at Clunie near Dunkeld in Perthshire. Arriving on the eve of their first wedding anniversary, he was the first child of Free Church minister, the Reverend Robert Macleod and his wife, Jane. Around his third birthday, the family moved to Keith in Banffshire where his father served the Free Church congregation for 4 years.

In 1883, at the age of 7, his family moved to Aberdeen. The Rev Macleod, a native of Caithness, had previously graduated MA from the University of Aberdeen and had studied Divinity at the Free Church College in Alford Place. He returned to the city to become minister at the John Knox Free Church in Gerrard Street which was to remain his charge – albeit in an imposing new granite building from 1895 – for over thirty years until he retired to Edinburgh in 1915.

The Macleod family lived initially at 86 Rosemount Place (now Belmuir House) throughout the time that JJR, usually known as Jack, attended Aberdeen Grammar School (1884-93) down Esslemont Avenue. In 1895, in the middle of his university studies, the Macleod family moved to a larger, newly built house named ‘Dunkeith’ (now 15 Kings Gate).

**University Education [1893-98]**

He entered the University of Aberdeen as an undergraduate in October 1893 having passed the University Preliminary Examination two weeks earlier. He excelled throughout the course (newly extended to five years) winning many prizes, including the Matthews Duncan medal in obstetrics that had been endowed by the highly distinguished medical practitioner James Matthews Duncan who, like Macleod, had been educated at Aberdeen Grammar School and the University of Aberdeen.

Macleod did his academic medical studies at Marischal College (before the front section of the current quadrangle was built at the start of last century) and in Aberdeen’s hospital facilities of the day. In the mid-1890s there was a recently opened Maternity Unit in nearby Barnett’s Close, out-patients were seen at the Public Dispensary across in Guestrow, infectious diseases were managed at the City Hospital in Urquhart Road, the Children’s Hospital was in Castle Terrace and the main Infirmary, with medical and surgical facilities, was at Woolmanhill. Macleod graduated MB ChB with Honourable Distinction in 1898.

**The Young Physiologist 1898-1903**

He competed successfully for the Anderson Scholarship which funded a year’s research in the Physiologische Insitut in Leipzig. He then returned to work in Aberdeen for a time, before moving to the London Hospital Medical College in October 1900, first as demonstrator in physiology and later lecturer in the emerging field of biochemistry. Over three years he published research on a variety of areas in the emerging field of clinical chemistry and was additionally appointed as Chemist to the Pathological institute at the London Hospital. He was also developing what were to become major interests in teaching, including the publication of textbooks.

**Appointed Professor in Ohio at 26 - 1903**

The early endeavours and achievements of Macleod as both researcher and teacher led in 1903, while still only 26 years of age, to his being invited to apply for the Chair of Physiology at Western Reserve University, Cleveland, Ohio. He was offered the post in June, was married in July to Mary Watson McWalter (a 2nd cousin from Paisley), and the couple sailed from Glasgow on 28th August to a new life in the New World. Macleod’s success continued over the 15 years he spent in Cleveland. His physiology and biochemistry teaching was highly regarded by his students; he put particular emphasis on practical classes as a means of teaching. His research was also successful and varied but, perhaps after writing a textbook chapter on the subject in 1906, became increasingly focussed on studies of carbohydrate metabolism and experimental diabetes. He developed a series of 8 lectures showing the relationship between his own research and on internationally published papers which led to his book called Diabetes: Its Pathological Physiology in 1913. A series of 12 publications on his original studies in the field were published over 10 years to 1917 in the American Journal of Physiology. He became a member of several prestigious societies (including in Germany and Italy!) and was invited widely to talk on his work – including a presentation at the meeting of the British Medical Association held in Aberdeen a few weeks before the outbreak of war in 1914. He contributed to the war effort from 1916 with studies on gas masks, aviation physiology, food conservation and societal nutrition. He was completing work on the first edition of a highly successful textbook called *Physiology and Biochemistry in Modern Medicine* (for which he wrote 90% of the chapters.

**Move to Toronto – 1918**

By the time his new textbook was published late in 1918, Macleod had left Cleveland and moved to the University of Toronto which had been trying for two years to persuade him to join as Professor of Physiology and to help with the redevelopment of their medical course; perhaps it is no coincidence that by 1927 it was to become the number one North American medical college. Macleod and is wife set up house at 45 Nanton Avenue in the Rosedale district of Toronto. The year after his move, Macleod was elected Fellow of the Royal Society of Canada and in 1920 began seven years as Associate Dean at his university. He continued with scientific presentations and publications at home and abroad based on his research studies on topics including effects of heat and cold exposure, metabolic acidosis, lactate measurement and regulation of blood sugar. His career as a research physiologist and as an innovative teacher continued to blossom – but he could not have imagined to what heights it was about to progress.

**Introduction to the Toronto Insulin Story 1921-22**

Several accounts have been written of this magnificent tale, the most comprehensively researched being the relatively recent book, ‘The Discovery of Insulin’ published by Toronto history professor, Michael Bliss in 1982. There were four main participants each of whom brought important attributes to the table. Professor Macleod, as we have seen, was already an experienced researcher with an international reputation in the field of the pathophysiology of diabetes. Bertram Collip, a Toronto graduate, was a professor of biochemistry in Alberta who was to spend several months doing research in Macleod’s department in 1921. Charles Best was a physiology student of Macleod graduating BA in late spring 1921 and due to do a summer attachment before continuing university studies in the autumn.

**Macleod’s Visit from Banting (8th Nov 1920)**

The story however is often focussed on the 4th participant, Frederick Banting and his big idea. Born on a farm in Ontario in 1892, he studied medicine in Toronto where his class were rushed through final year to graduate early in late 2016 so they could contribute to the war effort. Banting spent time working in military hospitals in England before being sent to the front. With the rank of Captain, he was awarded a Military Cross for bravery under fire at Cambrai and received a shrapnel wound to his arm which ended his active service. After recovering in England, he spent time in the military hospital in Toronto before being demobbed. He then had a year of surgical training but was not offered a further post in surgery and so set up a general practice in London, Ontario. Business was slow and he undertook some teaching to supplement his income. While preparing a lecture on the pancreas and studying relevant books and journals he one night came up with an idea that might allow preparation of an extract for treating diabetes. He was directed by his seniors to consult with Macleod, a world expert on the subject, in nearby Toronto – and they met in November 1920.

**Diabetes in 1920 – the background**

It is worth pointing out the situation as regards diabetes, and the search for a treatment at this time. There were no useful drugs available. Those developing the severe from of the condition (known nowadays as Type 1 diabetes) were typically children and young adults. The diagnosis was effectively a death sentence with survival mostly in terms of a few months. The only treatment, a very sparse diet amounting to near starvation, was for many worse than the disease. It had seemed likely since 1889 that a defect in the pancreas may cause some kinds of diabetes. Many groups had tried to isolate a pancreatic extract that could lower the blood sugar in experimental animals. Some – including Rennie & Fraser in Aberdeen experimenting with fish pancreas in the early 1900s – had even tried extracts on patients with diabetes. A few extracts had temporarily shown some lowering of blood sugar but all were too toxic to be tolerated for more than a day or two. Many doubted whether there would ever be a useful pancreas extract produced. Some hope for those researching in diabetes came with the recent development of techniques for measuring sugar on small amounts of blood which made repeat testing a possibility.

**The project begins (May 1921)**

Despite Banting’s lack of research experience and limited knowledge of the subject, Macleod continued his habit of encouraging young researchers and invited Banting to come to his laboratory for a few weeks the following summer where he would be given lab space, a student assistant and some dogs to work on. In May 1921, Banting arrived in Toronto and had meetings with Macleod to discuss the plan of research – and the Professor demonstrated the techniques of pancreas surgery on an anaesthetised dog. Charles Best was to be Banting’s assistant and the pair set out on a few weeks of experiments. The techniques were difficult and numerous dogs died during or shortly after surgery. Their skills improved, however, and by the end of July, they had successfully prepared an extract that was shown to lower the blood glucose in a diabetic dog. The extract was impure and not well tolerated such that most dogs receiving it did not survive for very long.

**Some success – and some difficulties (late summer 1921)**

By this stage, Banting was already totally convinced that he was the first to discover what would become known as insulin. He was apparently unaware that his big idea had been tried many years before (and was a complicated, unnecessary step) and also unaware that a number of researchers had already got this far with pancreas extracts – even using them (briefly!) in human diabetes – but all of the extracts so far produced were toxic and could not be tolerated by the dogs, or diabetic patients, receiving them. He resented Macleod’s experienced advice that repeated and more rigorous studies would be needed to produce safely reliable results. This was the beginning of what was to become lifelong suspicion and paranoia over Macleod’s motivation.

**Towards longer survival and purer extracts (late 1921)**

Macleod provided resources and facilities to allow Banting and Best to continue their studies, regularly advising on the necessary steps. The results were rather mixed but hopeful, especially when they were able to keep a dog alive for several weeks after removal of its pancreas. The problem remained of purifying an extract sufficiently to allow its use in diabetes patients and that is where Bertram Collip’s crucial contribution came into play. By December, Collip joined the team to work on the preparation of alcohol extracts, as advised by Macleod, with less contaminating and toxic contents. Collip also conducted studies to show the extract could reverse other abnormalities than high glucose levels in diabetic dogs, and developed a method using rabbits to measure the potency of different batches of extract.

**An Effective Treatment for Diabetes (January 1922)**

By the end of December 1921, the group was ready to present its preliminary results to the American Physiological Society. Banting gave the talk but public speaking did not come easy to him and support from Macleod – who was chairing the meeting session – was once again perceived by anting as the professor wanting to steal his success. Banting had been so concerned about the progress Collip was making that he had given his and Best’s extract by mouth to a diabetic patient in December; it had no effect. Banting next insisted on having their extract given by injection to a patient on 11th January when it had a slight effect on sugar but quickly produced abscesses where injected and so had to be abandoned. Collip meantime forged ahead with his experiments and soon had a cleaner and more potent extract ready for trial. On 23rd January 1922, Collip’s extract was injected into a patient in the late stages of exhaustion and wasting due to diabetes. The extract had a dramatic effect on the patient’s blood glucose levels and general well-being and clinically useful insulin had at last been discovered!

**Insulin – Finding Out and Sharing with the World**

Amidst the miraculous resurrections effected by the long sought for life-saving treatment for diabetes - soon to be known as *insulin* – an extraordinary amount of work still had to be done. Macleod turned over all of his research laboratory and staff to investigating insulin’s physiological properties. He took the lead in organising the dissemination of the news of the discovery – but let Banting and Best be named as the first two authors on the initial paper on the discovery in the Journal of the Canadian Medical Association and, unusual for the head of a research department, declined to have his own name included. There were problems in maintaining supplies and soon collaboration with the American pharmaceutical firm of Eli Lilly was established to facilitate mass production. A University of Toronto patent was taken out and Macleod ensured that arrangements were also made for production in Europe, that in the UK being overseen by the British Medical Research Council.

**Who got the credit – and who deserved it?**

In reflecting on who deserved the credit for bringing useful insulin to the world, Professor Michael Bliss of Toronto concluded in his definitive 1982 history, ‘The Discovery of Insulin’, that Banting, Best, Collip and Macleod all deserved a share of the credit. It was true that previous researchers had found pancreatic extracts that lowered glucose, mostly in diabetic dogs, but none had produced anything reliably suitable for treating diabetes. The labours of Banting and Best on their dogs through the hot summer of 1921 had undoubtedly driven the work forward and led to the production of a crude extract – but this barely matched the achievements of Zuelzer in Berlin in 1908. The input of Macleod – the internationally renowned expert on experimental physiology and diabetes – was central from the outset in advising and planning the research, in ensuring its proven scientific value, in evaluating the properties of insulin and in giving it to the world. Undoubtedly, the skill and industry of Collip in producing a purified version of the extract was a critical step in yielding a usable treatment.

At the time – and in subsequent decades, however, circumstances saw variable outcomes for the four participants. Banting continued to lobby against Macleod as having made virtually no contribution yet attempting to steal the glory. The legend grew of the Canadian farm boy having a great idea (which was neither original nor ultimately relevant) beating all the odds and making a great medical discovery despite the oppression of the professor. Banting was given a generous annuity by the Canadian Government and a Professorship with annual funds by the University of Toronto all designed to promote further research. After treating patients with insulin for about 2 years, Banting left diabetes to focus on research but made no major contributions to science. Best and Collip, who received no such acclaim – or funding - each made numerous scientific discoveries in their future work.

**The Nobel Prize 1923**

The Nobel Committee recognised the major breakthrough made by the discovery of usable insulin and in 1923, unusually quickly after the discovery, jointly awarded the Nobel Prize for Medicine or Physiology to Banting and Macleod. Banting was furious at Macleod’s inclusion and almost refused to accept. Neither Best nor Collip had been nominated; the rules allow a maximum of 3 scientists sharing an award. Banting shared his prize money with Best; Macleod shared his with Collip. Banting, still totally (and misguidedly) convinced that his idea and work was all-important, continued to complain about the trivial contribution of Macleod, the world famous professor who had allowed him facilities in his laboratory.

**Professor Macleod’s Return to Aberdeen**

Macleod continued his work as a teacher and administrator in the University, as an author and as a productive physiologist, including further research on insulin action and the potential of using fish insulin. However by 1928, perhaps having tolerated as much as he could of Banting’s jibes, he was pleased to return to his first university to take over the Regius Chair in Physiology in Aberdeen, replacing his own teacher, J A MacWilliam on his retirement. The return of a famous Nobel prize winner to his old university was hailed in the local press. He was involved in developments in physiology teaching and further research in his own department, with the Rowett Institute and the Torry Fishery Research Station on glycogen in liver and muscle, control of insulin secretion, absorption of nutrients and effects of temperature on metabolism in fish. He gave numerous lectures – including on a 2 month sabbatical in Baltimore as visiting professor of physiology at Johns Hopkins University in 1933. He welcomed many visiting researchers to his Aberdeen department from places including India, China, North America and Europe. He served on many local and national committees and was Dean of the Medical Faculty in Aberdeen, 1930-34. He was elected fellow of the Royal Society of Edinburgh in 1930. He also continued with scientific writing and editorial duties completing the 7th edition of *Physiology and Modern Medicine* in the winter of 1934/35.

**Declining Health**

First staying in Woodlands, Cults he supervised the building of a new house called Craigievar at the western extremity of Cults where he and his wife moved on its completion in 1930. Outside pursuits included membership of the MacDonald Trust Art Committee of the Art Gallery in Aberdeen, Associate Membership of the Aberdeen Medico-Chirurgical Society and Presidency of Aberdeen Grammar School Former Pupils Club. Unfortunately not long after his return to Aberdeen he suffered from increasingly disabling arthritis which, by the middle of 1933, would greatly curtail his ability to work and to travel. Latterly limited to his writing while being cared for and working from home, he died of cardiorespiratory problems on Saturday 16th March 1935 aged just 58 years. This was major news in the local press, not least because a fellow University professor died suddenly on the same day. A detailed account of their joint funeral at Kings College appeared in the Press and Journal a few days later. Macleod was buried in Allenvale Cemetery overlooking the River Dee

**Macleod Remembered – At last!**

It is a great surprise to many that Macleod and his stellar achievements are so little known in Aberdeen and beyond. There can be no doubt that Banting’s campaigning in Toronto against Macleod was a major contributor to this – at least until his death in a plane crash in Newfoundland in 1941 after setting out on a military visit to Britain. Following that, Charles Best, who had become an eminent physiologist in his own right, continued to promote the story of how ‘Banting & Best’ had made the important discovery. In fact, it has been described how he even favoured a Best & Banting version of their importance! Macleod’s achievements were not remembered or celebrated in the University where he had first studied and later been Professor of Physiology. That changed substantially in 1982 with the publication of ‘The Discovery of Insulin’ by Professor Michael Bliss, a University of Toronto historian. Bliss reviewed many detailed documents pertaining to the 1921 researches and met people who had known or worked with the main players, and some of the first patients who had survived almost 60 years as a result of insulin treatment. While acknowledging the contributions of the four main players in Toronto, Bliss’s book clearly shows how it was Macleod’s academic experience, unrivalled knowledge and scientific wisdom that guided this group, at this time, to achieve the elusive, life-saving treatment for diabetes. It was fitting therefore that the official opening of the JJR Macleod Centre for Diabetes, Endocrinology and Metabolism on Aberdeen’s Foresterhill campus was performed by Professor Bliss on 1st November 2013.