

Medical History

Robert Alexander McCance, and his forays into Experimental Medicine with Elsie Widdowson.

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RA McCance was born in Dunmurry and, after naval air service in the First World War and time on a dairy farm, went to Sidney Sussex College in Cambridge with the intention of taking the Diploma in Agriculture. However, he was persuaded that a career in medicine might be more practicable and after success in the Natural Sciences Tripos he worked with Gowland Hopkins for three years. As a married medical student in London he studied the use of the recently discovered insulin in gainful employment with RD Lawrence in King's College, where in the Hospital kitchen he met Elsie Widdowson in 1929. This was the start of a life-long collaboration, typified by their classic textbook 'The Chemical Composition of Foods'. Onerous work was no problem to the pair, and a lengthy investigation of fluid and electrolyte balance in adults kept on a salt-free diet for 14 days led him to examine renal function in infants. He was surprised to find that growth aided homeostasis by reducing the load on the kidneys.

Iron metabolism in polycythaemia revealed that iron regulation is achieved by excretion not absorption, and the resultant paper led to an invitation to him and his small team to set up a laboratory in Cambridge in 1938. Supplemental calcium with 85 per cent wholemeal brown bread was shown to provide a healthy diet in wartime rationing – and led to an invitation to describe the work in Dublin in January 1944. Survival at sea had become a problem of national importance and the team proved conclusively that sea water should not be drunk by mariners (when potable water supplies ran out). They also showed the importance of avoiding hypothermia after immersion in seawater. After twenty years as Professor of Experimental Science at Cambridge from 1945 to 1966, retirement was no more than an official term: the effects of wartime shortages on children in Germany and infant malnutrition in East Africa were examined in detailed studies. McCance recovered well after a cycling accident in Cambridge, but a fall in his home was more difficult to overcome, and he died in 1993. Elsie survived him by seven years until 2000.

INTRODUCTION

In the pleasant countryside of County Antrim south-west of Belfast Robert Alexander McCance was born on 9 December 1898 to John Stoupe Finlay McCance and Mary Letitia

Bristow. John trained as a barrister, but returned from Dublin to manage the family linen works in Dunmurry. His two brothers, Finlay and Harry, had been educated at St. Bees, Cumbria, and like them Robert made the short trip, aged 13, from Woodbourne, Dunmurry, across the Irish Sea after his schooling in Mourne Grange, Kilkeel, County Down. He retained great affection for St Bees and later became a Governor. A younger sister, Elizabeth, completed the family. After service in 1918 as a pilot with the Royal Naval Air Service, which involved hair-raising take-offs from primitive launching platforms, he worked for six months in 1919 at the County Farm near Antrim (town) before setting off for Sidney Sussex College, Cambridge, in October. Uncertainty in a rebellious Ireland persuaded him to take the Natural Sciences Tripos instead of his original choice of the Diploma in Agriculture – this was not agriculture's loss for his life's work never moved far away from that field, even if it was fundamental rather than applied. The professor of physiology, his fellow Ulsterman Joseph Barcroft (1872-1947), who was at that juncture preparing for his expedition to Cerro de Pasco in the Peruvian Andes, won his admiration. Barcroft's fundamental work on the respiratory function of the blood was of crucial interest to medicine and may have been an influence in the selection of medicine by McCance when agriculture was not feasible.

THE LIGHTS OF LONDON

Earning enough as a supervisor in physiology, he married a student at Girton College, Mary Lindsay MacGregor, in 1922, and after three years work in biochemistry and a PhD under Gowland Hopkins (FRS, Nobel Prize 1929, 1861-1947), he moved to King's College, London, to finish his medical studies. He obtained his M.B. in 1927, and M.D. in 1929. M.R.C.P. followed in 1930 and F.R.C.P. in 1935. Meanwhile laboratory work was not neglected for he analysed food samples for RD Lawrence.¹ The discovery of insulin in the summer of 1921 increased the importance of knowledge of the carbohydrate content of cooked fruit and vegetables,

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and McCance separated the available carbohydrates (sugar, dextrans and starch) from the polysaccharides nowadays designated as dietary fibre.² The Medical Research Council (MRC) was duly impressed and provided funds for a detailed study of the composition of meat and fish, as he encountered them in the hospital kitchen. The results were published in 1933 as the Medical Research Council Special Report No. 187 'The Chemistry of Flesh Foods and their Losses on Cooking' by R. A. McCance and H. L. Shipp.



Fig 1. Woodbourne House, Dunmurry, in later use as a hotel.

Source: <http://tuckdb.org/postcards/19695>, reproduced under the terms of the Creative Commons (<http://creativecommons.org/licenses/by-sa/3.0/>)

Into this milieu strayed his lifelong collaborator, Elsie Widdowson (21 October 1908-14 June 2000). At her school in Dulwich, southeast London, the chemistry mistress persuaded Elsie to take chemistry rather than zoology when she went on to Imperial College in 1925. After graduation she worked for Helen Archbold (later Helen Porter FRS, 1899-1987) for three years leading to her PhD on the changes in the individual carbohydrates in apples as they mature, ripen and are stored. In 1932 she spent a year working in the Middlesex Hospital with Professor EC Dodds (1899-1973), who advised her to take the one-year postgraduate course in dietetics – the up-and-coming profession – at King's College. As a preliminary she was sent to learn something about large-scale cooking in the main kitchen at the hospital. Luck is often better than skilful planning, and one day Elsie plucked up courage to speak to McCance, who told her about his current and earlier work. And, *mirabile dictu*, Elsie had enough courage to inform him that his figures for carbohydrate in fruit were too low, for some of the fructose must have been destroyed by acid hydrolysis. The gentleman scholar was not offended, but got a grant from the MRC so that she could join him while allowing her to finish the Dietetics Diploma.³ It was Elsie who recognised the need for British food tables, and this was the start of a long collaboration with McCance which culminated in their classic textbook, running to many editions: *McCance and Widdowson's Composition of Foods*.⁴

Diabetic coma was hazardous for the physician as well as the patient. One of the problems to be solved was the absence of chloride from the urine, and this observation led to experimental and quantitative study of salt deficiency.

Man is the best person to employ in this type of research and McCance decided to use him – a 'herculean' task for it involved persuading healthy young men and women to continue on a tasteless, unpalatable salt-free diet, and lie and sweat under radiant heat on a macintosh sheet for two hours every day for 14 days. The salt loss was measured by washing the subjects, and their sheets with distilled water after each session and analysing the washings; water loss was measured by weight loss.⁵ When they were salt deficient renal function was tested in various tests; the old adage that horses sweat, men perspire and women glow was borne out by one female student was unable to lose more than about a litre of sweat in two hours and never became seriously salt-deficient.⁶ These experiments helped clinicians to attend to the roles of fluids and electrolytes, and to remember the dictum of one of McCance's favourites Claude Bernard (1813-1878), that 'the stability of the internal environment is the condition of the free life';⁷ the fundamental difference between two medical specialties is that the investigator is interested in his problem, the physician in his patient.⁸

McCance was allowed some beds for his patients in King's College Hospital about 1934, and when his house physician, Winifred Young (1909-1969), moved to the Children's Hospital in Birmingham she continued the practice of testing the patients' urine and was surprised to find almost no chloride therein. When she reported these results to her King's College friends they were taken aback that even in full-term infants renal function was poor compared to adults. In animals as well as in man newborns were capable of maintaining homeostasis provided they were growing on a suitable diet – the milk of the mother, and so did not present a heavy load to the kidneys.⁹

THE CALL TO CAMBRIDGE

A woman admitted with polycythaemia rubra vera inadvertently changed the course of history when McCance and his colleagues reported that intravenous acetylphenylhydrazine (which lysed the red cells) did not cause the release of iron into the urine. They confirmed in themselves that iron is not regulated by excretion but by controlled absorption.¹⁰ The account, when it was published in the *Lancet* in 1937, led to an invitation to McCance to join John Ryle (1889-1950), the Regius Professor of Physic, as Reader in Medicine at Cambridge with a Fellowship in his old College. The offer was accepted on condition that the team of Elsie Widdowson and technician Alec Haynes also moved. The transfer took place during the Munich crisis in September 1938 and the first year was spent in completing the food tables and their study of children's diets.^{1,3}

When war broke out in September 1939 problem solving had to take on a more practical than academic bent. As Chairman of a joint MRC and Royal Naval Committee on the Care of Shipwrecked Personnel set up in 1941 which commissioned much research (continuing long after the war ended), McCance helped establish that sea water should never be drunk in response to dehydration after shipwreck.¹¹ Sea

sickness responded best to L-hyoscine, after the trials were moved from the (uncooperative) Atlantic to Portsmouth. As a bonus it was realised that 100g of glucose, cane sugar, or even boiled sweets were metabolised to 100g water – items more easily incorporated in survival rations. Sudden immersion in freezing water was another problem investigated, and the considerable individual differences in effect were not consistently explained by body fat. The collaborators' post-war studies (continuing into the 1950s) revealed the huge importance of hypothermia in accelerating death in these conditions. McCance himself was at the heart of this work, often carried out on small vessels in fierce Atlantic gales.¹²



Fig 2. Mourne Grange School, Kilkeel, Co. Down as it appeared in the early 20th century:

Source: the National Library of Ireland collection, http://catalogue.nli.ie/Record/EAS_1299, reproduction rights owned by the National Library of Ireland, reproduced under the terms of the Creative Commons CC0 1.0 Universal Public Domain Dedication.

But food supplies, nutrition and rationing assumed prime importance. A study of rationing was initiated in eight 'in-house' volunteers to see how far home-grown food would suffice for supplying the population. Milk, meat, eggs and other delicacies were reduced 'intolerably': total weekly allowances per person were four ounces of fat, five ounces of sugar (*in toto*), one egg, four ounces of cheese, six ounces of fruit, sixteen ounces of meat and fish combined, and one and three-quarter pints of milk per day. Wholemeal bread and vegetables including potatoes were not rationed. Physical fitness, tested during a trip to the Lake District, did not suffer, and the main conclusion was that calcium supply (already low, rations of milk and cheese being small) was further impaired by a constituent of brown bread – phytic acid. So a long series of balance experiments measured mineral intake and excretion in 10 subjects (over 3 or 4 weeks individually) lasting nearly a year as the subjects rotated through the five kinds of bread. Vitamin D did not improve the intestinal absorption, but fortifying the flour with calcium carbonate did, and the practice was later adopted nationally – in spite of the crank Isaac Harris's *The calcium bread scandal*.^{1,13} Mandatory addition of calcium to flour produced in the United Kingdom, and its beneficial effects on the skeletal health of the nation's children to be sustained through their adult lives, continues to the present day.

Elsie Widdowson recalled:

Somehow, Professor Jessop got to hear of our experiments and we were invited to describe them to a group of doctors and politicians including the Taoiseach, Mr De Valera. As a result it was decided to lower the extraction rate of flour used for bread-making [from 100% to 85%] in Eire, and later to add calcium phosphate to it, and the incidence of rickets in children over one year was decreased.³

WJE (Jerry) Jessop (1903-1980) was professor of biochemistry at the Royal College of Surgeons in Ireland when the Cambridge pair came over to Dublin in January 1944; he later headed the Department of Social and Preventive Medicine in his alma mater, Trinity College Dublin.

THE EUROPEAN DIMENSION

In 1945, McCance became the first Professor of Experimental Medicine in the UK, holding the chair in Cambridge until his retirement in 1966. The MRC sponsored a visit to post-war Germany to see what effects war-time rationing and food shortages had on children. The six month visit extended to three years when Elsie and Rex Dean found a suitable orphanage at Duisburg under the care of Dorothy Rosenbaum, 30 miles from their headquarters at Wuppertal in the Rhineland.

The underweight and under-height children, between 5 and 14 years, gained weight and height equally rapidly on bread made from all five types of flour: 100% (whole meal), 85% and 72% extraction (white), and white enriched with B vitamins and iron to the amounts in 100% and 85% extraction flour. All flour contained added calcium carbonate. Bread provided 75 per cent of the energy, and the diets contained only 8g of animal protein per day. The experiment lasted for 18 months; the children improved physically, and it was impossible for the outsider to tell what kind of bread the child had been eating.¹⁴

One girl from each group travelled – to their delight – with Elsie to the annual meeting of the BMA in Cambridge in 1949. After a frosty start, this interlude went very smoothly through the assistance of Dr Dorothy Rosenbaum who had an English mother and herself spoke colloquial English: "Here, you can't go up there". (p 31)³ During the war the professor had kept pigs near his home at Bartlow 16 miles from Cambridge, and the pigsties were there in 1949 when the team returned from Germany. This was the first programme to use experimental animals – and lasted 16 years. Pigs were so severely undernourished from 10 days of age that at 1 year they weighed 5 or 6 kg (without any body fat to keep them warm) when they would normally have scaled 200 kg. They recovered well and gained weight when given more food but they never outclassed their litter mates, although they mated successfully and their offspring gave no hint of their parents' deprivation. Their ability to recover from such a degree of malnutrition and put on weight was undoubtedly a tribute to animal husbandry as practised by Terry Cowen at Bartlow. The professor arrived at Terry's home one Sunday

afternoon to interview him for the post but left without giving a decision, until a month later he called and told the youth it was about time he started work. ‘When?’ I asked, ‘Thursday sounds a good day’.¹

Elsie Widdowson remained at Cambridge, continuing to study the effects of undernutrition of pigs, when McCance retired from his professorship in 1966. That was the year his wife died, and he travelled to Uganda to supervise the Medical Research Council Infantile Malnutrition Research Unit in Kampala. To approach the problems of malnutrition he was assisted by a paediatrician, Dr Brian Wharton, and an old friend from his boyhood in Dunmurry, Tom Hall, a retired Public Health Officer. The protein deficiency in kwashiorkor was more difficult to remedy than marasmus, for the marasmic children were very hungry and had little trouble taking the food they needed. The wards that were very hot in daytime got very cold at night; blankets provided the remedy.

¹ Observing bird- and wild-life was a welcome bonus.



Fig 3. From left to right: Dr. R.A. McCance, Mr. E. de Valera and Dr. E.M. Widdowson attending a meeting arranged by the Dietetic Council of the Irish Medical Association at the Royal College of Physicians in Dublin on 20th January 1944 to discuss “the nutritive value of bread of various extractions”.

(With thanks to Irish Newspaper Archives and The Irish Press.)

Returning to England in 1968, his last twenty five years were spent in Cambridge in touch with academic life in Sidney Sussex College, cycling up to twenty miles a day in the city and countryside until he was knocked off his bicycle on Midsummer Common by a woman pedestrian in the 1970s. But he still enjoyed pedestrian life until disabled about 10 years later by a fall, down the stairs from his flat, which forced him into sheltered accommodation. He continued to write and publish on nutrition, mineral metabolism and physiology until his last paper (entitled ‘The birth and early development of infant physiology’) appeared in 1992. He died on 5 March 1993.¹⁵

McCance was elected Fellow of the Royal Society in 1948 and appointed

CBE (Commander of the Order of the British Empire) in the New Year Honours for 1953 in recognition of the national

importance of his work, but he was also not without honour in his native land. Queen’s University in Belfast honoured him with a DSc in 1964. John Cowley, who spent a sabbatical year in Cambridge in 1962, and taught in Queen’s from 1968 to 1975, recalled: ‘When he visited us it was not unknown country and he was able to see some of his boyhood haunts, ... the world of nature and adventure’.¹

AN ALLIANCE MADE IN HEAVEN.

Elsie reminisced that ‘RA and I used to go to the [King’s College] hospital kitchen in the basement to get the big joints cooked in the hospital oven’. ‘There’, as he said himself in 1993, ‘I encountered Elsie Widdowson, a momentous meeting, for we have now remained together for 60 years’.¹

‘Those who worked with McCance, according to Elsie, loved his little eccentricities and many stories were told about them, some of them true, but others greatly exaggerated’. Romaine Hervey ‘never worked with Elsie but remembered her mainly in the *interface* between McCance and the outside world; she was a great soother of nerves in the Department and was intensely loyal to the professor’.¹ Douglas Black (1913-2002) worked in the department when Isaac Harris opposed McCance’s scientific evidence for adding calcium to bread: ‘Mac used to rage about Harris [and his booklet *The calcium bread scandal*], and about millers who didn’t want to add calcium to the flour, and Elsie would have to calm him down’.¹ In their first walk together in the Harz mountains in Germany, Eric Glazer (d 1992) realised that Mac was

‘a truly remarkable man; and it took longer and a more gradual understanding to realise that Elsie was no less remarkable. ... It took me some time to conclude that both contributed equally to their phenomenally successful partnership, though each provided different aspects of their work. There is no remote relevance in such suggestions as “Elsie does the work, Mac does the talking”, or that other extreme, “Elsie is a good technician dragged along by Mac’s genius”. The talents are entirely complementary. ... The result is a perfect blend of their talents in which the effect is far greater than a mere summation of their skills’.¹

Hamad Elneil, from Khartoum put it in a nutshell: ‘The professor provided the *breadth* for a project, and Elsie provided the *depth*’.¹ An Ulsterman, Ashton B Morrison, added a hard-headed note that ‘the professor was never a diplomat, and was capable of making the most critical, but often accurate, remarks about colleagues. Worse still, he sometimes made them rather directly ... a very brilliant man who could, at times, be difficult. He had a certain winning charm ... and Dr. Widdowson, fortunately, ... was always there to keep things going and to act as an arbitrator’.¹

In 1968 her own distinguished career continued with her appointment as head of the Infant Nutrition Research Division of the Medical Research Council’s Dunn Nutrition Laboratory. On her retirement from that post in 1973, she went on to work in the Department of Investigative Medicine (formerly

Professor McCance's Department of Experimental Medicine) at Addenbrooke's Hospital in Cambridge until 1988 when Professor Ivor Mills retired from the Chair. Ten years later, the Elsie Widdowson Laboratory was set up in Cambridge to house an MRC Unit for Human Nutrition Research, and in 2000 the newly-created Food Standards Agency included the Elsie Widdowson Library in their new headquarters in London. At various times Dr Widdowson was President of the British Nutrition Foundation, the Nutrition Society and the Neonatal Society.¹⁶ She died at Addenbrooke's Hospital after suffering a stroke while on holiday in Ireland.

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