EGON KODICEK

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Obituary Notice

EGON KODICEK, CBE, FRS, MD, PhD
(1908–1982)

Following the Gowland Hopkins tradition, Egon Kodicek immersed himself in research in Cambridge with the firm conviction that the disciplines of biochemistry and nutrition were an indivisible continuum. For 34 years he applied this belief at the Dunn Nutritional Laboratory: for the last 10 of those years, as its Director. This approach led to the unravelling of many molecular mysteries, yielding knowledge applicable to biology in general and to medical and nutritional problems in particular.

On 27 July 1982, at the age of 73, greatly honoured for his achievements but frustrated by still unrealized ambition, Egon Kodicek died. He was a man who quite late in life had the opportunity of demonstrating that his own unique style of biological investigation could indeed solve intractable problems. His controversial concept of nutrition, appearing revolutionary to some, but heretical and dangerous to others, formed the basis for a remarkably productive and fertile decade of discovery.

Kodicek was brought up in a medical household, his father being a doctor at Kamenny Ujezd in Bohemia where Egon Hynek Kodicek was born on 3 August 1908. After studying medicine at Charles University in Prague he graduated with an MD in 1932 and for the next 7 years combined the practice of medicine with research on vitamins and hormones at the University's Department of Internal Medicine. During this time he developed links with the University Institutes for Pathology and for Animal Biology, as well as with the Czechoslovak State Institute of Public Health. A collaboration with Professor J. Heyrovsky at the Physicochemical Institute was of particular significance as it laid down the mental framework for his future research. At this stage Kodicek's early studies were already recognized for their imaginative originality. He was awarded prizes for his work in the fields of internal disease and physicochemistry and he received as well the Masaryk Fund Prize of the Czechoslovak National Research Council.

Fortunately, before the beginning of World War II, his reputation had reached Britain. As the Nazi invasion spread throughout Czechoslovakia, Kodicek, as a Jewish academic, was in fear of his life. Along with other European Jewish scientists he was offered sanctuary in Britain where he fled after terrifying encounters with the Gestapo which left an indelible impression on his personality. In June 1939 he arrived in Cambridge and, as a Scholar of the Society for the Protection of Science and Learning, he began work at the Dunn Nutritional Laboratory under the aegis of the University of Cambridge and the Medical Research Council (MRC). In 1942 he was appointed to the Scientific Staff of the MRC and became a permanent member in 1947. It was in the Dunn that he established his mark on nutritional science and developed his distinctive research style.

The philosophical basis of Kodicek's research was the application of physicochemical knowledge to biology. He was fascinated by the concept of vitamins: that minute quantities of such small molecules could have profound effects on whole-animal biochemistry and physiology. With Heyrovsky he had studied the polarographic properties of ascorbic and folic acids to devise methods of detecting and measuring their concentration in tissues. Using this technique he was the first to realize that vitamin B_{12} contained an inorganic cation which he tentatively identified as either cobalt or copper. The development of methods for measuring vitamins occupied much of his time during the first 10 years in Cambridge. He

devised chemical and fluorimetric assays for riboflavin and nicotinic acid and for the metabolites, *N*-methyl nicotinamide and the pyridine nucleotides. He discovered that much of the nicotinic acid in cereals was nutritionally unavailable, being covalently bound to a poorly digested and complex macromolecule termed 'niacytin'. The biochemical consequences of the lack of a vitamin also attracted his attention and he began studies on collagen and mucopolysaccharide formation in vitamin C deficiency, as well as studies on the biochemical changes associated with deficiencies of riboflavin, folic acid and pyridoxine.

By 1950 he had accepted the challenge of vitamin D – the biochemical function of which was completely unknown. After ingeniously devising microbiological and reversed-phase-chromatography assays for vitamin D, Kodicek concluded that the quantity of vitamin D which was physiologically active was an order of magnitude less than any other vitamin. He decided that a new hypothesis was needed to explore the function of fat-soluble vitamins in general and vitamin D in particular, and he postulated that vitamin D was a 'catalytic surfactant' which acted by specifically modifying the surface pressure of cell membranes, so changing their permeability. He realized that chemical assays for vitamin D were too insensitive and that vitamin D function in vivo could only be investigated with assays using the radioactively-labelled molecule. Therefore he set about biosynthesizing [^{14}C]ergocalciferol using yeast and then later, with the assistance of Dr R. K. Callow, a range of tritium-labelled cholecalciferols was prepared.

It was from this stage that Kodicek's studies became increasingly unconventional for a nutritional laboratory. In searching for a simple model of vitamin D action he developed his interests in membranes and lipid metabolism in bacteria and supported investigations which led to the discovery of the isoprenoid alcohol 'bactoprenol' in *Lactobacillus* spp. To assist these new lines of research new equipment was needed but this was obtained only with the greatest of difficulty. In later years Kodicek delighted in telling of his struggle for funds to purchase a scintillation spectrometer and a high-speed, refrigerated centrifuge. The 'Packard' and the 'Spinco' had become symbols of a breakdown in the boundaries of nutritional research.

In 1962 the MRC was beginning to contemplate the fate of the Dunn Nutritional Laboratory after the retirement of Dr L. J. Harris, who had been Director since the Laboratory was established in 1929. It was widely felt at that time that because most nutrients were identified and because the amounts of these needed to maintain health were approximately defined, further research in nutrition should have a low priority. However, during the assessment of the Dunn the visiting MRC committee came across a scholarly gentleman in an undistinguished back room who presented them with a visionary concept of a role for nutrition in future medical research. To his amazement, the MRC invited Egon Kodicek to put forward a research programme and to take over as Director in 1963. He accepted this new challenge and it was agreed that the Laboratory should expand both its technical resources and in the scope of its research.

After becoming Director, Kodicek's ideas of nutrition emerged in a more tangible form for those around him. He viewed biological and medical problems as problems of cell function. The whole animal was the cell writ large and nutritional research was a study of the influence of the external chemical environment upon the activities of this multitude of cells. Hence, with his physicochemical approach, he was intrigued by membrane phenomena in cells: how simple and complex nutrients were transported across cell membranes, and the influence of nutrition on how cells secreted and excreted their metabolic products. He saw in the future, the complete integration of nutritional knowledge with that of other medical disciplines in an assault on the unsolved ills of mankind.

During the first years as Director, Kodicek enthusiastically supervised the design and construction of a new building which increased the facilities for modern biochemical

research. How excited Dame Harriette Chick and Sir Rudolph Peters were to see the gleaming new equipment when they jointly performed the opening ceremony in 1968. Under Kodicek's expanded view of nutrition, scientists who previously would not have considered a nutritional laboratory as a likely venue for their research were attracted to work at the Dunn. Thus apart from chemists and biochemists, additional expertise was acquired in microbiology, experimental pathology and electron microscopy. The range of topics was further enlarged by the incorporation of Dr Elsie Widdowson's team studying problems of infant nutrition.

The main aim in Kodicek's plan of research was to create an environment where good people were happy and could communicate with their chosen problems and with each other. He would support and encourage his team of scientists in the use of their own ideas and skills. If, as so often happened, an unpredicted and inexplicable observation was made he eagerly encouraged further experimentation until the explanation was apparent. It was of no concern if the chase led to regions far removed from nutrition for Kodicek abhorred the restrictive codification of science. Unfashionable as the view now is, he strongly believed that if one supported fine minds working in areas of ignorance, the most useful results were more often obtained by the vigilant scrutiny of chance findings rather than by the logical attempt to solve pre-defined problems.

How true this was of the research on vitamin D. His original hypothesis of its function as a catalytic surfactant is now believed to be wrong. Yet this concept enabled him to bring together a research team to try to determine experimentally the mechanism of action of vitamin D. They began by attempting to locate where vitamin D went within cells, believing, once again erroneously, that the molecule acted without metabolic transformation. It was only the serendipitous discovery of the loss of tritium from [1α-^{3}H]cholecalciferol that led to the realization that vitamin D underwent two hydroxylation reactions. The second of these reactions was discovered, again by chance, to take place in the kidney. This revealed that vitamin D had in fact an endocrine function mediated by a new renal metabolite, 1,25-dihydroxycholecalciferol.

Further valuable, but completely unpredicted, information came from the studies he initiated on the bound nicotinic acid in cereals. It was demonstrated that in niacin-deficient rats this bound nicotinic acid appeared ultimately in urine as an abnormal metabolite, trigonelline. This led to the discovery that the intestinal mucosa had an increased permeability to large molecules in niacin deficiency. Subsequently, much later work showed that this mucosal lesion in rats resulted from a sensitivity to gluten, in a manner analogous to human coeliac disease.

While many other significant findings, in connective tissue metabolism, on ribosomal structure and on bacterial cell wall synthesis, were made during Kodicek's tenure as Director, he became well-known mainly because of the Laboratory's work on vitamin D. For this he received many honours, from France, Switzerland, Italy, the USA and Czechoslovakia, as well as receiving the British Nutrition Foundation Prize in 1973 and the Ciba Medal of the Biochemical Society in 1974. He was in constant demand as a Chairman of government, MRC, international, and United Nations committees on nutrition and he was Vice-President of the Group of European Nutritionists in 1971 and President of the Nutrition Society from 1971 to 1974. His election as Fellow of the Royal Society came in his final year as Director and he was made a Commander of the British Empire on his retirement.

Sadly, retirement was a heavy burden for Egon Kodicek. Although he was well supported to work on vitamin D at the Strangeways Research Laboratory in Cambridge his enthusiasm had waned and he was plagued by ill health. He dearly would have liked to have known what vitamin D was doing in muscle but the physical effort of setting up

experiments had become too much. For him the golden years were as head of a large, lively and productive laboratory. At the end of the Kodicek era, with an increasing demand for public accountability of research funds and with a trend towards customer-relevant research, it was almost inevitable for the MRC to decide that investigations on nutrition should revert to more traditional and human-related studies. This disturbed Egon Kodicek greatly. Perhaps he hoped that he had founded a new school of nutritional research. He did not quite grasp that his real legacy was the magical influence he had had in stimulating and enthusing his scientific colleagues.

What was it about 'Kodi' that made him such a stimulating scientist? His youthful enthusiasm in keeping abreast of new developments was maintained throughout his working life. This gave him a great breadth of knowledge and shrewd judgement of where the answers to research problems might lie. At the end of a tedious day of administrative nonsense, nothing refreshed him more than sitting late in the Laboratory with young people, discussing their research. His eyes would gleam and his fingers demolished one paper clip after another as the day's 'great thought' began to evolve. Even though the ideas were sometimes wrong, he inspired the minds of those around him and correct solutions would ultimately emerge.

Kodi's friendliness and warmth have become a legend among the countless visitors he received and entertained from around the world. He was devoted to his charming and remarkable wife, Jindra, who for 55 years sustained him in troubled times and rejoiced with him in his triumphs. There must be many with delightful memories of the hospitality they so generously gave together at their home in Bulstrode Gardens.

Scientist, teacher, philosopher: what was the strong motivation that drove Egon Kodicek to success? Like others tinged with greatness it was simply a search for the truth. For him, scientific research was not an occupation, but an intuitive, creative art. As the mysteries of vitamin D began to unravel, his pleasure and satisfaction were revealed in his own words: 'It is not only an interesting scientific story, but also an "aesthetic" one, as is always the case when the truth in Nature is discovered.'

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