



OBITUARY

Michael J Stock (1942–2001): an appreciation

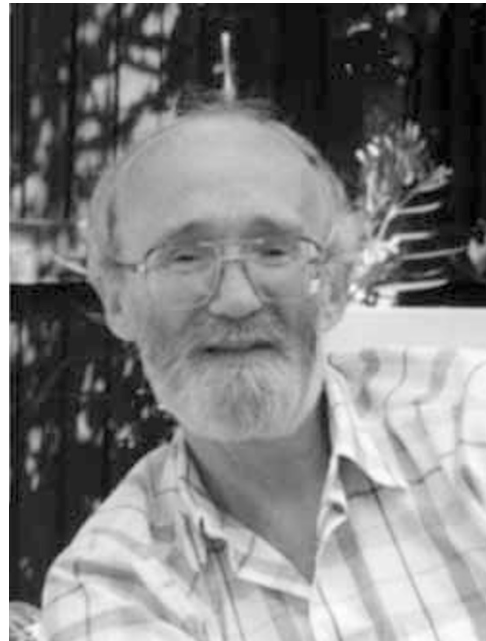
Obesity research has lost one of its foremost scientists, and one who played an especially pioneering and innovative role. Michael John Stock died on 26 March 2001 at the early age of 58, following a long battle with cancer which he had fought with remarkable resilience and fortitude.

Mike Stock was born in London in 1942 at the height of the Second World War. His route into science was through a position as a Junior Technical Officer in the Human Nutrition Research Unit at the National Institute of Medical Research in London. From there he went to the University of Sheffield where he obtained a First Class Honours Degree in Physiology. This was followed by a PhD in the Nutrition Department at Queen Elizabeth College, University of London, under the supervision of Derek Miller. He was appointed to a Lectureship in the Physiology Department at Queen Elizabeth in 1969, where he remained for 10 y until his appointment in 1979 to a Senior Lectureship in Physiology at St George's Hospital Medical School, University of London. His move to St George's was a rather special event, documented in the BBC *Horizon* film *Fat in the Fire*. Who else can say that their relocation to a new academic position was portrayed in an influential television programme and broadcast across a number of countries?

Mike Stock remained at St George's for the rest of his life, being promoted to a Readership (1981) and then to a Professorship (1986). He assumed the role of Acting Head of the Physiology Department between 1989 and 1990 and was Head from 1998 until his death.

During his career at Queen Elizabeth College and at St George's he supervised a total of 22 postgraduate students. The first of these was Ian Macdonald, current Editor of the *International Journal of Obesity*. His fourth student was Nancy Rothwell, now MRC Research Professor at the University of Manchester, with whom he had a remarkable scientific collaboration. Indeed, between the time of her PhD and her departure to Manchester several years later 'Rothwell and Stock' became a formidable duo. Formidable for their innovation, their productivity and their influence—and for the sheer passion and belief in what they were doing.

Mike Stock was a disciple of Derek Miller, another iconoclastic scientist and much of his work, like that of Miller, centred on trying to establish the importance of variations in energy expenditure—and of diet-induced thermogenesis in particular—in the regulation of energy balance and the aetiology of obesity. This view was to reach its zenith through the development by Mike Stock and Nancy Rothwell of the cafeteria-fed rat as a model to explore the



metabolic response to overfeeding. Rats presented with a variety of palatable human-type foods will voluntarily overeat and the degree of hyperphagia can be such that the metabolisable energy intake may be up to two-fold higher than in rats fed a standard laboratory diet. In some circumstances, much of the excess intake is not deposited as lipid but rather is expended—diet-induced thermogenesis. At the time these results provided the most compelling evidence for the existence of a regulatory process in energy balance which depended on adaptive changes in expenditure.

The observations on diet-induced thermogenesis in cafeteria rats were not without controversy. Indeed, in certain quarters they were the subject of heated debate and were attacked with ferocity, most notably by Romaine Hervey and Graham Tobin at the University of Leeds in the UK. The reasons for the scale of the hostility are still difficult to understand. Some of the scepticism was, however, in part a consequence of the variability of diet-induced thermogenesis, a number of factors (including the strain, age and sex of the rats, and the environmental temperature at which the experiments are conducted) influencing the extent of the process. For example, studies conducted on adult female rats at thermoneutrality give rather different results from those involving young male rats at 20°C. Undoubtedly, underlying

the hostility was the widely held traditional view that physiological systems operate at maximum efficiency with minimal energy wastage.

After developing the cafeteria diet as a simple overfeeding regimen, the pivotal contribution that Mike Stock made was in demonstrating (with Nancy Rothwell) that in rodents brown adipose tissue is a key site of adaptive diet-induced thermogenesis. This work was reported in a major article in *Nature* in 1979,¹ showing a functional hypertrophy of brown fat in animals exhibiting diet-induced thermogenesis on a cafeteria diet. This article has been highly influential, and has received more than 1000 citations. It followed important papers by two Canadian Groups; one was the demonstration by David Foster and Lorraine Frydman, using radioactively labelled microspheres to map regional blood flow, that brown adipose tissue is the major site of thermoregulatory non-shivering thermogenesis in cold-acclimated rats. Shortly afterwards, Jean Himms-Hagen and Michel Desautels reported that the activity of the proton conductance pathway in brown adipose tissue mitochondria (the mechanism by which heat is produced in the tissue) is reduced in genetically obese (*ob/ob*) mice.

In a collaborative study with Paul Trayhurn and Anne Goodbody in Cambridge, Mike Stock and Nancy Rothwell found that the activity of the proton conductance pathway is stimulated in rats overfeeding on a cafeteria diet. This provided powerful evidence to support the proposition that diet-induced thermogenesis is mechanistically the same as non-shivering thermogenesis. The genesis of this study was a high point in my own research career. Several of those interested in the then putative link between brown fat and energy regulation were invited by Ed Schönbaum to the Fourth Symposium on the 'Pharmacology of Thermoregulation', which was held in Oxford in July–August 1979. In addition to Mike Stock and Nancy Rothwell, this included Jon Arch, Jean Himms-Hagen and myself. In the afternoon following the close of the meeting, Mike Stock, Nancy Rothwell, Jean Himms-Hagen and I retired to a small pub off Holywell Street. In the indolent atmosphere of Oxford on a hot and humid August day we discussed the emerging ideas on brown fat as a mediator in the regulation of energy balance and the development of obesity. Ideas tumbled out, particularly from Mike Stock, and a collaboration between London and Cambridge to examine whether the proton conductance pathway was activated in rats exhibiting diet-induced thermogenesis was agreed. This collaboration led to a joint paper in *Nature* and featured in the first half of the '*Fat in the Fire*' film referred to earlier.

In a series of seminal studies, Mike Stock and Nancy Rothwell established that the sympathetic nervous system is the key mediator of the activation of brown fat heat production in diet-induced thermogenesis and the involvement of different hormonal factors, particularly insulin and glucocorticoids, was also established. For several years their productivity was breathtaking, both in terms of the conduct of experiments and the rate of publication. At the time

'Rothwell and Stock'—as they were generally known—rivalled some of the great historical partnerships in biology.

Mike Stock was one of those scientists whose achievements received stronger recognition outside his own country. In the 1980s, when diet-induced thermogenesis and brown adipose tissue were at their most topical and controversial, he was widely sought as a speaker at international meetings and travelled frequently. It was principally within the UK that his ideas were regarded as heretical in some influential quarters and attacked ferociously. There is little doubt that for a while he was damaged by the attacks, and he did not receive the level of grant support from the major UK Research Councils that his originality and productivity required. Indeed, it is probable that in most other scientifically advanced countries he would have received considerably more recognition and support. This was despite one of the enduring characteristics of the 'brown fat community'—mutual respect and a certain solidarity (reflecting the sense of the beleaguered that characterised the field at times).

Mike Stock was, however, the recipient of the prestigious Wasserman Prize at the 9th European Congress of Obesity in Milan in 1999, and this was very welcome recognition of his enormous contribution. He gave what many felt to be a truly outstanding presentation, and as one who had heard him speak on a number of occasions there was no doubt that his Wasserman Lecture was in a very special category; indeed, it was a model of everything that a Prize Lecture should be. It was even more impressive in that because of his escalating cancer he was having increasing difficulty in speaking. The lecture was subsequently published in the *International Journal of Obesity*.²

Most of Mike Stock's career involved studies on experimental animals, which enable full energy balance to be assessed—a requirement still frequently overlooked in the field. He did, however, have forays into human work, including studies on physiological adaptations to high altitude. Thus he was the Leader of the 1984 Anglo-Italian Monte Rosa High Altitude Project and was involved scientifically in polar expeditions. In his last few years he developed an interest in leptin, and together with some of his colleagues secured two major grants from the Wellcome Trust. It is fitting that eventually he received substantial support from the world's largest Research Charity. In the previous decade most of his research funds came from the pharmaceutical industry. Although this was most welcome and reflected the scientific esteem in which he was held by what are highly discriminating organisations, the work was focused on the effects of putative anti-obesity agents, restricting the extent to which he could give full rein to his creativity. Nevertheless, he was able to make a number of important contributions and by the end of his life he had published a total of 161 papers, most of which are in leading journals, and more than 70 review articles.

Mike Stock served the broader scientific community in several direct ways, most notably as a successful Chairman of the Association for the Study of Obesity in the UK and as

Editor-in-Chief and subsequently Executive Editor of the *International Journal of Obesity*. He was also a member of the Editorial Board of the *American Journal of Physiology* and of the Advisory Board of the *British Journal of Nutrition*. Together with Trevor Silverstone he organised the 2nd European Congress on Obesity in Oxford in 1989 and served on the Scientific Committee of several successive European Congresses—the 7th, 8th, 9th and 10th—as well as the last two International Congresses (Toronto 1994 and Paris 1998).

A workshop was held in honour of Mike Stock in Richmond, London, on 21 April 2001. When the idea of holding such a meeting after his death was made, as it became clear that his long fight against cancer was not to be successful, Mike Stock's response was typical of the man '... waiting until I've gone—I want to be there!'. It was therefore arranged for a few weeks after he received the news that he did not have long to live, and his friends were hopeful that he would be present. Sadly, that was not to be the case. A small group of friends and close colleagues came for the meeting from the UK, mainland Europe and North America, reflecting the considerable affection and esteem in which Mike Stock was held. An occasion worthy of him took place, the substance of which has been reported elsewhere in this issue of the *International Journal of Obesity* by Ian Macdonald and Nancy Rothwell. Mike would have drawn quiet satisfaction from the extent to which much of what he fought for scientifically is now widely accepted.

The cover of the workshop programme reproduced telling words from Omar Khayan, and these were Mike's chosen epitaph:

'Make the most of what ye yet may spend,
Before you too into the dust descend'

Mike Stock was rare among scientists and his death is a considerable loss. He will long be remembered both as an engaging person and as a highly influential scientist. He is survived by his wife, Elizabeth Evans, who is also professionally involved in obesity, and by a son and two daughters.

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References

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- 2 Stock MJ. Gluttony and thermogenesis revisited. *Int J Obes Relat Metab Disord* 1999; **23**: 1105–1117.