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Waterlow J C, Garlick P J & Millward D J. *Protein turnover in mammalian tissues and in the whole body.* Amsterdam, The Netherlands: North-Holland. 1978. 804 p.
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The aim of this book was threefold: to give a comprehensive account of the principles and problems of measuring protein turnover in the whole body and in tissues *in vivo*; to examine critically the pros and cons of different methods and the assumptions on which they are based; and to summarize the information on these subjects that was available at that time (1978), with special emphasis on results obtained in humans. [The *SCI*® indicates that this book has been cited in over 725 publications.]

Charting the Biochemistry of Malnutrition

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In the 1950s I was doing clinical research on severely malnourished children in Jamaica. In spite of everything, many of them died. I had the idea that if the machinery for protein synthesis was impaired, it would lead to an irreversible state. So how could we measure the capacity of these children to synthesize protein? The first measurements of whole body protein turnover in humans had been made by D.B. Sprinson and R. Rittenberg[1] in 1949. However, by the 1960s this line of work had petered out, probably because it had an unsound theoretical basis. Intuitively, I felt that a sounder approach would be to use a continuous infusion of isotope and what I learnt later is called stochastic analysis, which does not depend on knowing the internal structure of the system. There was nothing very original about this idea.

In 1961 I was able to spend three years in London, doing animal experiments that would provide the basis for studies on protein turnover in children. My colleague, Joan Stephen, and I were given hospitality by Professor A. Neuberger in a part of his laboratory at St. Mary's Hospital. We worked in a place called the Mint Stables, because it originally housed the horses that delivered the mail from Paddington Station. Neuberger, a most distinguished biochemist, encouraged us because he had been interested in nutrition since his war service in India.

We measured free and protein-bound lysine in rat tissues with lysine decarboxylase in the Cartesian diver. This is a gasometric instrument like the Warburg but 1 000 times more sensitive. I was an enthusiast for the method. I had constructed the apparatus myself, and one of my first papers was on its application to measurements on biopsy samples of human liver.[2] At St. Mary's we were joined by Peter J. Garlick, a fresh graduate from Cambridge, who was prepared to risk taking his PhD under these rather primitive conditions. He provided the mathematical basis of the equations for measuring synthesis rates.

For work on children we would clearly have to use a stable isotope. The Wellcome Trust, with great foresight, provided us with a mass spectrometer for the work in Jamaica, and Drs. John Garrow and James Halliday got this going in the face of great difficulties such as power cuts and other problems of the kind so common in the Third World. Many people thought we were crazy to try to use advanced technology under such conditions, but it paid off. When I returned to Jamaica in 1964, Dr. David Picou, one of the first batch of medical graduates of the University of the West Indies, started the studies with ^{15}N-glycine in children that led to our first paper on protein turnover in humans.[3] At this time also we were joined by D.J. Millward, another young graduate from Cardiff, who continued the experimental work that was necessary to enlarge our understanding, since quantitative measurements of protein synthesis rates *in vivo* were still few and far between.

As a result of our papers on lysine turnover,[4,5] I was invited to contribute an article to *Physiological Reviews*. Since I had approached the subject as a clinician, I felt that our group had at last established ourselves scientifically, and I was immensely pleased. However, the article was rejected, and the referee refused to make any reply to my responses to his criticisms. This was a bitter blow, and I contemplated giving up the whole line of work. Again Neuberger came to the rescue and persuaded Elsevier to commission a book. Such was the genesis of the book that is the subject of this commentary. It has not been republished, but a small attempt has been made to bring it up to date.[6]

1. **Sprinson D B & Rittenberg R.** The rate of interaction of the amino acids of the diet with tissue proteins. *J. Biol. Chem.* 180:715-26, 1949. (Cited 110 times.)
2. **Waterlow J C.** Oxidative phosphorylation in the livers of normal and malnourished human infants. *Proc. Roy. Soc. London Ser. B* 155:96-114, 1961. (Cited 20 times.)
3. **Picou D & Taylor-Roberts T.** The measurement of total protein synthesis and catabolism and nitrogen turnover in infants in different nutritional states and receiving different amounts of dietary protein. *Clin. Sci.* 36:283-96, 1969. (Cited 215 times.)
4. **Waterlow J C.** Lysine turnover in man measured by intravenous infusion of L (U-^{14}C) lysine. *Clin. Sci.* 33:507-15, 1967. (Cited 70 times.)
5. **Waterlow J C & Stephen J M L.** The effect of low protein diets on the turnover rates of serum, liver and muscle proteins in the rat, measured by continuous infusion of L-^{14}C lysine. *Clin. Sci.* 35:287-305, 1968. (Cited 270 times.)
6. **Waterlow J C.** Protein turnover with special reference to man. *Quart. J. Exp. Physiol.* 69:409-38, 1984. (Cited 35 times.)