

This Week's Citation Classic

Campbell R M, Cuthbertson D P, Matthews C M & McFarlane A S. Behaviour of ^{14}C - and ^{131}I -labelled plasma proteins in the rat. *Int. J. Appl. Radiat. Isotop.* **1**:66-84, 1956. [Rowett Inst., Bucksburn, Aberdeenshire, Scotland and Nat. Inst. Med. Res., Mill Hill, London, England]

From the urinary excretion curves of ^{131}I of separately labelled pure proteins by the rat and from total activities in the extravascular compartment it seems the metabolic breakdown of albumin and γ -globulin occurs in the intravascular compartment, but these proteins are metabolised independently. [The *SCI*[®] indicates that this paper has been cited over 190 times since 1961.]

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"During 1954-55 a longstanding friendship and common interest in the metabolism of the plasma proteins drew together myself, director of the Rowett Research Institute (RRI), Aberdeen, and A. S. McFarlane, head of biophysics at the National Institute for Medical Research (NIMR), London. We then had the assistance, respectively, of Rosa Campbell and Christine Matthews.

"I was primarily keen to study the metabolism of the plasma proteins following injury, for in collaboration with the late S. L. Tompsett I had earlier published a note.¹ Does injury 'produce both the disposition and means of cure'?² McFarlane, on the other hand, was more interested in the behaviour of the plasma proteins in disease. How would they differ? It was therefore decided to pool our respective techniques. Because of some 500

miles between the two centres it was arranged that the animal work would be done at RRI and the preparative and analytical work on the proteins at NIMR. It was first necessary to determine the metabolism of the plasma proteins in normal conditions using ^{131}I -albumin and globulins of demonstrable purity. In the rat, which is more constant in behaviour than the rabbit, we found that the ^{14}C and ^{131}I -labelled proteins behaved in substantially the same way. But the specific activity curve of the total proteins in rat plasma could not at any time be expressed as a single exponential curve. Curves for individual plasma proteins were almost truly exponential for five to 15 days after injecting the labelled molecules. Applying the necessary corrections for growth and plasma sampling, equivalent apparent replacement rates were calculated. The excretion curves for ^{131}I in the first few days after injecting ^{131}I -albumin suggested that albumin and γ -globulin are broken down mainly, if not exclusively, in close proximity to the circulating plasma. Urinary and plasma data were interpreted to mean that rat plasma proteins are metabolised by essentially independent processes.

"In this research a new method was introduced for determining the mass distribution of proteins in both intra- and extravascular compartments and an illustration was provided of the use of total body γ -radiation measurement for studying the metabolism of ^{131}I -labelled plasma proteins.

"Readers have obviously been impressed by the meticulous care exercised in this research and have used it as a pattern, thus accounting for its frequent citation."

1. Cuthbertson D P & Tompsett S L. Note on the effect of injury on the level of the plasma proteins. *Brit. J. Exp. Pathol.* **16**:471-5. 1935.

2. Hunter J. *A treatise on the blood, inflammation and gunshot wounds*. London: Nicol, 1794. 575 p.