This Week's Citation Classic

CC/NUMBER 49
DECEMBER 8,1980

Hales C N & Randle P J. Immunoassay of insulin with insulin-antibody precipitate. *Biochemical J.* **88**:137-46, 1963.
[Department of Biochemistry, University of Cambridge, Cambridge, England]

The authors describe a radioimmunoassay for insulin employing a solid phase reagent of guinea pig insulin antibody pre-precipitated with rabbit antiguinea pig γ-globulin serum. Sensitisation of the assay by pre-incubation with unknown or standard prior to addition of radiolabelled hormone is described. The assay proved suitable for the development of a commercial kit. [The *SCI*® indicates that this paper has been cited over 2,240 times since 1963.]

C. N. Hales
Department of Clinical Biochemistry
Addenbrooke's Hospital
Cambridge CB2 2QR
England
and
P.J. Randle
Nuffield Department of
Clinical Biochemistry
University of Oxford
Radcliffe Infirmary
Oxford OX2 6HE
England

October 20, 1980

"Whilst it is superficially pleasing to find this paper highly cited according to the *Science* *Citation Index*® *(SCI®),* explaining the occurrence may serve to illustrate an important limitation of the *SCI* as an indicator of the real scientific importance of a paper. Our contribution describes one of the many modifications introduced to the original radioimmunoassay of Yalow & Berson.[1] Undoubtedly, if every paper dependent on results obtained by radioimmunoassay were to refer to the true originators of the concept, Yalow & Berson's paper would be at or near the top of the *SCI* and the latter would then much more faithfully reflect the real value of their contribution. Fortunately, this achievement has been acknowledged by the award of the Nobel prize to Yalow, though it is a matter for regret that Berson did not live to share this recognition.

"Our own struggles to set up a radioimmunoassay for insulin led us at a very early stage to appreciate the need for a readily available technique for clinical research and to attempt to persuade commercial organisations to supply the reagents. The reluctance of the latter to countenance the technique as originally described, led us to explore the use of alternative approaches based on the anti-immunoglobulin precipitation technique of Sköm & Talmage.[2] A highly convenient solid-phase reagent was prepared along the lines pioneered by Moloney.[3] The work reported in this paper represents part of the PhD thesis by one of us (C.N.H.). The technique formed the basis of studies of insulin secretion in diabetes and of studies independently by both of us on the control and mechanism of insulin secretion *in vitro.*

"It is interesting, in the light of the current commercial interest in radioimmunoassay and the commercial success achieved by marketing our method, to recall the reluctance of the firms approached to enter this field. The fact that British firms were the first to commercialise an American discovery makes a pleasant change. However, it is disappointing that this early lead was not exploited more successfully. (It might perhaps be worth stating in these days of increasing commercial arrangements between academic scientists and industry, that our initiative which led to the first commercial radioimmunoassay kit was not motivated by and did not result in any financial benefit to us).

"Thus one can suggest that the position of the paper in the *SCI* is due to a number of factors: the proven value of radioimmunoassay, the large volume of work in diabetes and in particular on insulin secretion, the robustness of the technique we devised and its commercial availability."

1. **Yalow R S & Berson S A**. Assay of plasma insulin in human subjects by immunological methods. *Nature* **184**:1648-9, 1959.
2. **Sköim J H & Talmage P W.** Nonprecipitating insulin antibodies. *J. Clin. Invest.* **37**:783-6. 1958.
3. **Moloney P J.** Endogenous and pancreatic insulins. *Ciba Found. Coll. Endocrinul.* **14**:169-81. I962.