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This Week's Citation Classic

Glick S M, Roth J, Yalow R S & Berson S A. The regulation of growth hormone secretion. *Recent Progress in Hormone Research* **21**:241-83, 1965. (Radioisotope Service, Veterans Administration Hospital, Bronx, NY]

Plasma radioimmunoassayable human growth hormone (HGH) levels fluctuate widely and rapidly in response to stimuli that have in common a shortage of carbohydrate energy substrate, and to stress. Glucose lowers plasma HGH in normals but not in acromegalics. The HGH response to insulin hypoglycemia distinguishes normals from hypopituitary subjects. [The *SCI*® indicates that this paper has been cited over 360 times since 1965.]

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This publication represented the summary of two exciting years in partnership' with Jesse Roth in the now famous laboratory of Sol Berson and Ros Yalow In 1961, just after their work on the radioimmunoassay (RIA) for insulin we were given the 'easy' job of developing a RIA for HGH But even under the guidance of the masters' and with a great deal of hard work, just the development of a reliable assay took us over a year.

'Being the only children' of the brilliant researchers and teachers, Berson and Yalow was an unforgettable experience They gave of themselves to us with their characteristic intensity and excellence —well beyond three standard deviations from the norm. We staggered home twice weekly after a three hour lecture by Sol on differential equations with mimeographed notes prepared just f*or the two of us.* Ros and Sol set an example of integrity, hard work and precision of thought that dazzled and depressed us We appreciated most their willingness to let us struggle independently with our project, with little interference —but with the knowledge that the experts were at our beck and call.

"Struggle we did. For months we were in the 'paper business.' Whatman 3MM paper, fine for insulin, did not do for HGH For a while we 'manufactured' our own composite brand — Whatman 3MM plus a site of application made up of DEAE paper. We spent hours on the floor of the lab gluing these components together.

"With the assay working, after improved hormone purification, we turned to physiology, in the search for stimuli and suppressors of HGH. The goal was the evaluation of clinical states of hyper- and hyposecretion. Fortunately, the first stimuli investigated included insulin hypoglycemia. The magnitude of the response surprised us, and we knew we had made a major discovery. The next few months were devoted to daily physiological experiments, many on ourselves and families. I learned that insulin hypoglycemia superimposed on a six day fast does not enhance one's feelings of well-being But walking across the Bronx with Jesse, discussing our next experiments was an exhilirating way of testing the effect of exercise on HGH.

"The work altered drastically the then prevalent view of growth hormone as a 'slowly moving' hormone involved largely in growth. The work stimulated much new thought regarding the physiology of growth hormone and its neuroendocrine control A direct means of measuring a pituitary hormone and its fluctuations was provided, and thereby a tool for assessing hypopituitarism and acromegaly. The breakthrough early in the course of the application of RIA to various new substances gave dramatic demonstration of the powerful tool developed by Berson and Yalow and its enormous potential for physiology and medicine. "