

This Week's Citation Classic

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Boyd A E, Lebovitz H E & Pfeiffer J B. Stimulation of human-growth-hormone secretion by L-dopa. *N. Engl. J. Med.* 283:1425-9, 1970.
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This paper showed clearly that the administration of L-dopa, a precursor of central nervous system catecholamines, stimulated the release of growth hormone in man. The data indicated that a dopaminergic mechanism in the median eminence or norepinephrine sensitive site in the hypothalamus was involved in human growth hormone regulation. [The *SCI*[®] indicates that this paper has been cited in over 360 publications since 1970.]

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"In 1969, I started an endocrine fellowship working with Harold Lebovitz at Duke University in Durham, North Carolina. I had just completed three years of training in medicine at Boston City Hospital and Duke after graduating from medical school at Washington University in St. Louis. Like many ideas in clinical medicine, the genesis of our studies on L-dopa was at the bedside. I saw a patient of John Pfeiffer who was taking a new experimental therapy, L-dopa, for Parkinson's disease. The patient was a mild diabetic and we worried about the effect of the new medication on his diabetes. We thought that this precursor of catecholamines might inhibit the release of the patient's endogenous insulin and result in deterioration of the diabetes. We set up a clinical study of Pfeiffer's patients to investigate the effect of L-dopa on glucose metabolism. When I reviewed the literature it also became obvious that this amino acid would cross the blood-brain barrier, increasing turnover of dopamine and norepinephrine in the hypothalamus, and could be used as a probe to study control of the pituitary by catecholamines. On the basis of the animal data in which amines had been injected directly into the ventricles or hypothalamus, I thought that L-dopa might stimulate the release of the gonadotropins. To our surprise, instead, L-dopa stimulated a

dramatic rise in growth hormone levels in the patients we studied, and it did not alter the pituitary hormones which control the adrenal, thyroid, or gonadal axis. The L-dopa-induced rise in growth hormone could not be blocked by either oral or intravenous glucose. This latter information was obtained serendipitously from the studies in which we had administered the drug prior to glucose, and subsequently measured insulin secretion. Since L-dopa was a precursor of both dopamine and norepinephrine, growth secretion appeared linked to dopamine pathways in the median eminence or norepinephrine in the hypothalamus. Subsequent studies by a number of investigators have indicated that both dopaminergic and noradrenergic pathways control the release of growth hormone by increasing the secretion of a putative growth hormone-releasing factor.

"In 1970 it was not clear that prolactin was a distinct human hormone, but in 1971 it became possible to measure serum prolactin levels in man,¹ and L-dopa was shown to have a potent inhibitory effect on prolactin secretion.² After our studies in parkinsonian patients, I enthusiastically recruited all of the endocrine fellows at Duke to come to Lebovitz's home on Sunday mornings to take the drug. L-dopa is a powerful emetic and my bloodletting was frequently interrupted by the rush of my friends to the bathroom. These studies were soon interrupted more definitely by my entering the Army after one year of fellowship.

"This publication is frequently cited because it was the first study to directly test the monoaminergic control of pituitary function in man. In addition, the L-dopa test has become a standard clinical means of evaluating growth hormone secretion. In acromegaly, a pituitary disorder with excess growth hormone secretion, L-dopa and dopamine agonists have a paradoxical effect lowering the elevated growth hormone levels and are now used to treat this disease. Similar success is seen in the therapy of disorders of excess prolactin secretion."

1. Martin J B. Neural regulation of growth hormone secretion. Medical progress report. *N. Engl. J. Med.* 288:1384-93, 1973.
2. Malarkey W B, Jacobs L S & Daughaday W H. Levodopa suppression of prolactin in non-puerperal galactorrhea. *N. Engl. J. Med.* 285:1160-3, 1971.