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Franz J. Ingelfinger, M.D.
To The Editor
The New England Journal of Medicine
10 Shattuck Street
Boston, Massachusetts 02115

Dear Sir:

METABOLIC RESPONSES TO LEVODOPA

The lead article by Sirtori et al (1) confirms Boyd et al in their discovery that growth hormone is released by single doses of levodopa in fasting patients (2). Their own contribution however lacks both the internal and the external consistency necessary for heralding responsibly a severe iatrogenic disease like acromegaly.

These authors are internally inconsistent as follows. They predict only harm from evoked releases of growth hormone, ignoring spontaneous releases of roughly similar magnitude found normally during sleep (3). They appear to be predicting the effects of the variable doses required for treatment, on the basis of fixed single morning doses given to fasting patients. Although not one of their baseline values was affected by chronic treatment with levodopa, those among their patients who exhibited some metabolic effect are posed as future prototypes for all patients. They find only a minor impairment of glucose utilization with compensatory hypersecretion of insulin, but sound an alarm which can cause irresponsible reactions. They seem to have forgotten already the severity of the diseases which levodopa relieves.

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These authors are also inconsistent externally. Clinical, radiological or metabolic evidence of acromegaly has not been reported by any of the investigators who have been puzzled by the significance of its absence for the two years elapsing since the discovery by Boyd et al (2). Some of our 105 patients with parkinsonism or chronic manganese poisoning have received dopa continuously for 7 years without the slightest evidence of "frank acromegaly". Furthermore, Mena et al at Brookhaven cannot confirm the implied extrapolations (from fixed single morning doses of levodopa in fasting subjects) to multiple daily therapeutic doses: large pulses of circulating growth hormone emerge thus far only after the first morning dose and, even then, their magnitude depends upon the patient's protein intake. That these pulses might even be therapeutically useful is suggested by our experiments with mice, in which bovine growth hormone has prolonged and potentiated the cerebral actions of levodopa (4). Life-long consumption of levodopa (20 mg/g Purina chow) has markedly prolonged the lives of mice in incomplete experiments by S.T. Miller, W.H. Maston and myself. Completion of these experiments requires two additional years, but they already argue strongly against the premonitions of Sirtori et al.

At present, levodopa is not only the single most effective remedy against two serious neurological diseases, but it also seems perhaps promising as a treatment for osteoporosis and for some cancers of the female breast. These authors might therefore "elevate them guns a little lower" as General Jackson once said.

Very sincerely yours,

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