EDITORIAL

GROWTH HORMONE: ANABOLIC AND ANTICATABOLIC AGENT

In a special article in this journal[1] R. Levine and R. Luft recently suggested that a substance AK (adipokinetic) may be present in growth hormone preparations, in addition to the anabolic agent itself, accounting for the fat-mobilizing and diabetogenic activities of such preparations. Although this proposal has some experimental support in earlier studies with animal pituitary extracts, studies with human growth hormone have thus far favored the view that there is only one biologically active substance, causing both growth and fatty acid mobilization. It may be prudent therefore to try to explain the apparent incongruities about growth hormone without invoking the "2-factor hypothesis."

The importance of growth hormone as a regulator of energy metabolism has been emphasized in recent studies. Growth hormone has been shown to cause a rise in plasma free fatty acids within two hours after injection and Roth, Glick, Yalow and Berson have shown that the growth hormone content of the blood increases rapidly in response to hypoglycemia, deoxyglucose and muscular exercise and increases slowly with fasting. The stimuli to growth hormone secretion are states in which fatty acids are needed as a source of energy and are therefore reasonable stimuli for the secretion of a fat-mobilizing substance. Excessive action of this type may take on a diabetogenic character when abundant availability of fatty acids reduces the oxidation of glucose markedly and encourages ketogenesis.

The fat mobilizing effect of growth hormone has been regarded, correctly, as glucose-sparing and calorie-providing, but it has not been sufficiently emphasized that it is also protein-sparing. When fatty acid release is viewed as an anticatabolic device, its promotion by an anabolic and growth-promoting agent becomes more understandable. Furthermore, the conditions that stimulate growth hormone secretion are, at least in the case of fasting and of muscular exercise, catabolic states.

Growth hormone may be regarded as having both an anabolic and anticatabolic function; fatty acid mobilization is part of the latter function. Fatty acids spare glucose, but this, during fasting, is equivalent to sparing protein, since the glucose which is spared would otherwise have to be replaced from amino acids. Fatty acids may also spare amino acids directly by reducing their oxidative metabolism. Anticatabolism may be further served by growth hormone through stimulation of protein synthesis from endogenous amino acids. The "diabetogenic" effect of growth hormone, which has seemed anomalous to the purpose of the hormone, may be thought of as the anticatabolic action carried to excess.

In this view, growth hormone is secreted in large amounts when the protein stores are threatened, and it acts to conserve protein. The daily accretion of protein during normal growth is small (perhaps 0.25 gm. of nitrogen in a nine-year-old child), and Levine and Luft argue that the caloric need for formation of new peptide bonds is small and that fat mobilization is therefore unnecessary. But the potential loss of protein during a fast is large and a source of many calories is needed to conserve body proteins in the absence of food.

The effectiveness of a growth-promoting agent may depend as much on its ability to conserve proteins between meals, as on its ability to promote the use of ingested nitrogen for protein synthesis. There need be no fear of excessive growth from large amounts of growth hormone during periods of catabolism since an actual increase in total body protein can occur only with exogenous nitrogen. Excessive growth, or acromegaly, appears to occur only when growth hormone secretion is continuously high, and is not suppressed, as it is in the normal individual, by food or glucose.

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[1] Levine, R., and Luft, R.: The relation between the growth and diabetogenic effects of the so-called growth hormone of the anterior pituitary. Diabetes 13:651, 1964.