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# Growth Hormone and the Lipolysis of Exercise

**Colin Currie B.Sc.**

**Abstract**
From a dissertation read before the Society on January 22nd. 1969.
Growth hormone (GH) is secreted by the acidophil cells of the anterior pituitary. It is a protein, partially α-helix in structure, of molecular weight 29,000 in man (1 ). In addition to its effect in promoting growth several metabolic effects follow its administration, one of which, the mobilisation of free fatty acid (FFA) from adipose tissue, will be discussed in some detail.

The radio-immunoassay methods for estimating GH (2, 3) which are the most sensitive and accurate now available, depend on the fact that radio-iodinated GH of high specific activity (4) competes with standard or test GH in plasma for binding sites on a γ-globulin in antiserum prepared in rabbits. The competition results in 'bound' and 'free' 131I-GH which are separable electrophoretically and counted for radio-activity. Inhibition curves relating bound: free ratios to standards are drawn and test samples assayed against them. There is good evidence that the assay is specific (5). Reactive material is elevated in acromegaly and is absent after hypophysectomy: jugular vein plasma contains more than inferior vena cava plasma: cross-reaction occurs between plasma samples only from species whose pituitaries contain cross-reactive material: acromegalic plasma acts just as a plasma dilution of pituitary extract.



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# GROWTH HORMONE AND THE LIPOLYSIS OF EXERCISE

**Colin Currie, B.Sc.**

*From a dissertation read before the Society on January 22nd, 1969*

Growth hormone (GH) is secreted by the acidophil cells of the anterior pituitary. It is a protein, partially $\alpha$-helix in strucure, of molecular weight 29,000 in man(1). In addition to its effect in promoting growth several metabolic effects follow its administration, one of which, the mobilisation of free fatty acid (FFA) from adipose tissue, will be discussed in some detail.

The radio-immunoassay methods for estimating GH (2, 3) which are the most sensitive and accurate now available, depend on the fact that radio-iodinated GH of high specific activity (4) competes with standard or test GH in plasma for binding sites on a 8-globulin in antiserum prepared in rabbits. The competition results in 'bound' and 'free' $^{131}$I-GH which are separable electrophoretically and counted for radio-activity. Inhibition curves relating bound : free ratios to standards are drawn and test samples assayed against them. There is good evidence that the assay is specific (5). Reactive material is elevated in acromegaly and is absent after hypophysectomy : jugular vein plasma contains more than inferior vena cava plasma : cross-reaction occurs between plasma samples only from species whose pituitaries contain cross-reactive material : acromegalic plasma acts just as a plasma dilution of pituitary extract.

The survival of GH in plasma has been investigated. Intra-venous injections of GH showed a half life of about 30 minutes (6, 7). Endogenous GH stimulated by hypoglycemia and 'switched off' by glucose and glucagon infusion (8) decreased at a simple exponential rate with a half time of 20-40 minutes.

Plasma GH levels show marked fluctuations. 'Spikes' occur in healthy adults fasting in bed (5). Variations influenced by exercise, nutritional state and sleep are such that only serial estimations on individual subjects give meaningful results about GH secretion (9).

A 70 kg. man may contain 350 g. of glucose and 10,000 g. of fat, yet the importance of FFA as a metabolic substrate has been recognised only recently (10, 11). Triglycerides in fat cells are hydrolysed to glycerol and FA by hormone sensitive lipases (12), glycerol being liberated to plasma and FA being bound to albumin for transport. Plasma glycerol (13) and FFA levels have both been used as an index of lipolysis. Many hormones initiate or contribute to lipolysis : adrenaline, noradrenaline, corticotropin, thyrotropin, thyroxin, corticosteroids, intermedin ($\alpha$ and $\beta$ forms), glucagon, vasopressin and GH.

*In vitro* methods have been widely used in the investigation of lipolysis : results must be evaluated with suspicion as awkward but

physiological complexities may be eliminated. However, isolated rat adipose tissue cells, subject to the combined actions of GH and a synthetic glucocorticoid showed a lipolysis that was slow in onset and secondary to RNA synthesis (14). The addition of Actinomycin D, which blocks protein synthesis, prevented the lipolysis. The inclusion of a protein-synthesis delay in the timing of the GH mediated lipolysis of exercise would prohibit any close short-term correlation to energy demands. Human subjects injected with exogenous GH show an initial fall then a delayed rise in plasma FA levels, the rise being maximal at about 4 hours (15, 16, 17).

When subjects perform moderate exercise their plasma FFA levels rise from the basal post-absorptive levels (18). In these experiments mean levels rose from 0.76 to 1.44 m. moles/litre. Turnover of FFA as measured by continuous infusion of palmitate-1-$C^{11}$ with measurement of specific activity of FFA and expired $CO_2$, is also increased in exercise (10). This increase is gradual and spread over the first hour of exercise, but uptake from the blood doubled almost immediately.

GH levels, too, rise in exercise. The very low basal levels in the resting postabsorptive state rise within an hour of the onset of exercise to a peak of total duration 1-2 hours. Prolonged exercise elicits more peaks. In these experiments (19) the FFA levels rose throughout exercise, but the times of onset of FFA and GH rises could not be compared on account of long sample intervals. Hartog *et al.* (20) using shorter intervals showed small transient depression of both GH and FFA in the first 10 minutes of exercise. Mobilisation of fat revealed by increased plasma glycerol, occurred within 5-10 minutes, whereas GH did not rise until after 20 minutes. This discrepancy in the timing of the two events would seem to eliminate GH at least from the initiation of the lipolysis of exercise.

The elegant human forearm preparations used by Rabinowitz *et al.* (21, 22) to study FA arterio-venous differences over subcutaneous and deep muscular vascular beds. Simultaneous R.Q. and glucose arterio-venous difference determination confirmed the importance of FA as a fuel for muscular exercise. Intra-arterial injection of GH in near-physiological concentrations produced a prompt increase in FA uptake by muscle : subcutaneous tissue released FA after a delay of about 40 minutes. These findings provide a possible basis for the observed fall and rise of plasma FA after GH administration. Once more the considerable latency in GH-induced lipolysis makes it an unlikely contributor to the FA rise of early exercise.

Some of the experiments quoted above arrive at conclusions based on changes in plasma levels, the significance of which should therefore be critically considered. The plasma level of a substance is the net effect of its addition to, and removal from, the blood : a change in plasma level reflects an excess of one over the other. The turnover of a substance may vary independently of its plasma level, e.g. in certain circumstances where lipolysis in adipose tissue and FA uptake by muscle are both raised, turnover will increase while plasma levels may remain constant. Similarly high plasma levels may conceal a low turnover. Hence future attention should be directed towards turnover studies with labelled FA combined with short interval GH estimation.

Plasma FA has a high turnover (10). The human forearm (21) and whole rat experiments (16) indicate that GH can cause an immediate fall in FFA, suggesting an increase in uptake. It is also established that GH causes a later rise in plasma FA attributed to lipolysis in adipose tissue. These two sets of observations make it exceedingly difficult to interpret changes in the plasma FA levels following GH administration or endogenous secretion. Since the hormone is associated with two antagonistic effects on plasma FA due to stimulation of uptake and release it is likely that the lipolytic action of GH might commence much earlier than the FFA rises observed by many workers (15, 23), and that an unchanged plasma FA level might conceal an increase in turnover. Such theoretical considerations provide a basis for the variety of latencies suggested for the lipolytic action of GH. The human forearm experiments eliminate the crude plasma levels and take separate account of uptake and release by measuring A-V differences across subcutaneous tissue, presumed adipose, and deep, muscular, vascular beds. The brief latency observed (40 minutes) is probably reliable.

Growth hormone is released by the anterior pituitary and is distributed to the systemic blood by the venous drainage of the gland and the jugular vein. Once more the instantaneous plasma levels tell nothing of its release and uptake. We do not know the duration of the burst of secretion which gives rise to the GH

peaks found in exercise or basal, fasting subjects. These last 1-2 hours (19, 20) and figures obtained from sampling at intervals of 10 minutes suggest that the rise is steep (20). Most of the rise may occur between two samples, perhaps reflecting pituitary activity lasting seconds, or, at most, minutes. Little significance can be attached to the height of these peaks. Mixing in the peripheral blood followed by distribution to the extracellular fluid and uptake by the tissues will determine the decline of the peak: these factors contribute to the observed half life in plasma, which is 20-30 minutes. This is fairly constant regardless of the physiological circumstances in which GH is administered, suggesting that uptake is not a variable (24). There is no information about its duration of action.

In general, hypothalamic-pituitary neuroendocrine systems mediate control between the CNS, where units of neural activity occupy only milliseconds, and the periphery, where metabolism and structure alter over minutes and years. When exercise commences, GH is liberated and lipolysis occurs. The events may be causally related. In any case, two latencies have to be considered: the first, before plasma GH levels rise, could conceivably be a case of simultaneous release and uptake as discussed above; or it could simply be a delayed GH response. If the former, turnover could be detected with labelled GH though difficult technical problems of estimation and short interval sampling would arise. The second delay, prior to the lipolysis which follows a close intra-arterial injection of GH (21), is well established. Together these latencies appear to disqualify GH from an adipokinetic role linked at all closely to the varying demands of exercise. However, *in vitro* evidence that GH facilitates lipolysis by other hormones (14, 25) suggests a synergistic role: in which case the time relations might be less important.

To summarise briefly: transient peaks in plasma GH levels are regularly seen in exercising adults. *In vitro* evidence suggests an association, involving other hormones, between GH and lipolysis. The maintenance of lipolysis in continuing exercise may depend in part on this effect. However, from the evidence concerning the onset of lipolysis and GH secretion on the commencement of exercise, it is not possible to conclude that GH secretion initiates lipolysis in exercise.

*REFERENCES*


1. Evans (1966). In "The Pituitary Gland". Ed: Harris and Donovan. Vol. 1, p. 439.
2. Hunter and Greenwood (1964). *Biochem. J., 91*, 43.
3. Glick (1963). *Nature. 199.* 784.
4. Li (1953). In "Ciba Foundation Colloquia in Endocrinology". Vol. 5, p. 115.
5. Glick (1965). *Rec. Prog. Hor. Res., 21.* 241.
6. Parker (1962). *J. clin. Invest., 41.* 262.
7. Laron (1965). *Nature, 207.* 298.
8. Glick (1963). *Clin. Res., 11.* 404.
9. Loraine (1966). In "Hormone Assays and their Clinical Application". p. 165.
10. Havel (1963). *J. clin. Invest., 42.* 1054.
11. Schlerss (1964). *Metabolism, 13.* 934.
12. Evans (1966). In "The Pituitary Gland". Ed: Harris and Donovan. Vol. 1, p. 454.
13. Borchgrevnik (1963). *Proc. Soc. exp. Biol., 113.* 946.
14. Fain (1965). *J. biol. Chem., 240.* 3522.
15. Beck (1960). *Metabolism, 9.* 699.
16. Zahnd (1960). *Proc. Soc. exp. Biol., 105,* 459.
17. Swislocki (1965). *Endocrinology, 76.* 664.
18. Basu (1960). *Quart. J. exp. Physiol., 45.* 312.
19. Hunter (1965). *Science, 150.* 1051.
20. Hartog (1966). *Quart. J. exp. Physiol., 52.* 86.
21. Rabinowitz (1962). *Clin. Res., 10,* 402.
22. Rabinowitz (1965). *J. clin. Invest., 44.* 51.
23. Raben (1959). *J. clin. Invest., 38.* 484.
24. Editorial (1909). *Lancet, 1,* 85.
25. Goodman (1964). *Proc. Soc. exp. Biol., 115.* 849.


## The Itch

Authors, and those too, of no small note contend for animalcules being the cause of this distemper; and indeed it is hard to call in question the veracity of such Gentlemen, who have given us not only the figure of these little creatures, but also assure us that, upon further search they discovered the Eggs from which they are produced by generation, as fast as Lice. Be this however as it will, I should give it as my opinion that still these animals are not to be looked upon as the cause, but rather the effect of this disease.

—*from the Society's collection of Dissertations, 1772.*