

Fasting enhances growth hormone secretion and amplifies the complex rhythms of growth hormone secretion in man.

[K Y Ho](#), [J D Veldhuis](#), [M L Johnson](#), [R Furlanetto](#), [W S Evans](#), [K G Alberti](#), and [M O Thorer](#)

Department of Internal Medicine, University of Virginia Medical School, Charlottesville 22908.

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Abstract

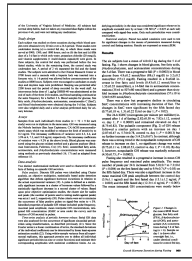
Studies in man have shown that the episodic release of growth hormone (GH) is infrequent and erratic, and unlike that in the rat does not appear to have discernible ultradian periodicities. However, these observations in nonfasted subjects may be invalid since mixed nutrients have unpredictable effects on GH release. Moreover, in the fed state basal GH levels are frequently undetectable, thus rendering the identification of low amplitude pulses unreliable. Accordingly, the 24-h pulsatile pattern of GH secretion obtained from repetitive venous sampling in six normal adult male subjects was examined during a control fed day and during the first and fifth days of a 5-d fast. The GH data were analyzed using two distinct methods: a discrete pulse detection algorithm (Cluster analysis) and Fourier expansion time-series, which allows fixed periodicities of secretory activity to be resolved. The 5-d fast resulted in a significant increase in discrete GH pulse frequency (5.8 +/- 0.7 vs. 9.9 +/- 0.7 pulses/24 h, $P = 0.028$), 24 h integrated GH concentration (2.82 +/- 0.50 vs. 8.75 +/- 0.82 micrograms.min/ml; $P = 0.0002$), and maximal pulse amplitude (5.9 +/- 1.1 vs. 12.3 +/- 1.6 ng/ml, P less than 0.005). While multiple low-amplitude sinusoidal periodicities were present on the control fed day, time-series analysis revealed enhancement of circadian and ultradian cycles on the first and fifth days of fasting. Concomitantly, fasting resulted in a decline (day 1 vs. day 5) in serum concentrations of somatomedin C (1.31 +/- 0.22 vs. 0.77 +/- 0.18 U/ml) and glucose (4.9 +/- 0.2 vs. 3.2 +/- 0.2 mmol/liter), and a marked rise in free fatty acid (0.43 +/- 0.12 vs. 1.55 +/- 0.35 mmol/liter) and acetoacetate (35 +/- 6 vs. 507 +/- 80 nmol/liter). We conclude that the acute nutritional status is an important determinant of spontaneous pulsatile GH secretion in man. Fast-induced enhancement of GH release is achieved through combined frequency (discrete pulses) and amplitude (sinusoidal periodicities) modulation. Such alterations in somatotrophic hormone release may play an important role in substrate homeostasis during starvation.

Full text

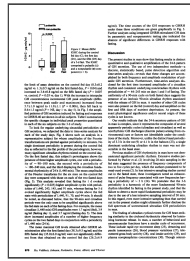
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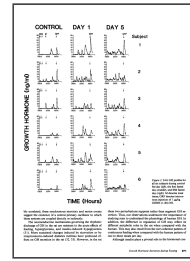
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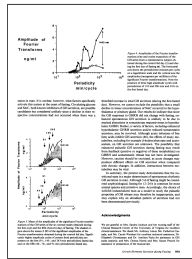
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Selected References

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- Takahashi Y, Kipnis DM, Daughaday WH. Growth hormone secretion during sleep. *J Clin Invest.* 1968 Sep;**47**(9):2079–2090. [[PMC free article](#)] [[PubMed](#)]
- Finkelstein JW, Roffwarg HP, Boyar RM, Kream J, Hellman L. Age-related change in the twenty-four-hour spontaneous secretion of growth hormone. *J Clin Endocrinol Metab.* 1972 Nov;**35**(5):665–670. [[PubMed](#)]
- Goldsmith SJ, Glick SM. Rhythmicity of human growth hormone secretion. *Mt Sinai J Med.* 1970 Jul-Aug;**37**(4):501–509. [[PubMed](#)]
- Ho KY, Evans WS, Blizzard RM, Veldhuis JD, Merriam GR, Samojlik E, Furlanetto R, Rogol AD, Kaiser DL, Thorner MO. Effects of sex and age on the 24-hour profile of growth hormone secretion in man: importance of endogenous estradiol concentrations. *J Clin Endocrinol Metab.* 1987 Jan;**64**(1):51–58. [[PubMed](#)]
- Quabbe HJ. Chronobiology of growth hormone secretion. *Chronobiologia.* 1977 Jul-Sep;**4**(3):217–246. [[PubMed](#)]
- Quabbe HJ, Schilling E, Helge H. Pattern of growth hormone secretion during a 24-hour fast in normal adults. *J Clin Endocrinol Metab.* 1966 Oct;**26**(10):1173–1177. [[PubMed](#)]
- ROTH J, GLICK SM, YALOW RS, BERSON SA. Secretion of human growth hormone: physiologic and experimental modification. *Metabolism.* 1963 Jul;**12**:577–579. [[PubMed](#)]
- Tannenbaum GS, Martin JB. Evidence for an endogenous ultradian rhythm governing growth hormone secretion in the rat. *Endocrinology.* 1976 Mar;**98**(3):562–570. [[PubMed](#)]
- Clemmons DR, Klibanski A, Underwood LE, McArthur JW, Ridgway EC, Beitins IZ, Van Wyk JJ. Reduction of plasma immunoreactive somatomedin C during fasting in humans. *J Clin Endocrinol Metab.* 1981 Dec;**53**(6):1247–1250. [[PubMed](#)]
- Berelowitz M, Szabo M, Frohman LA, Firestone S, Chu L, Hintz RL. Somatomedin-C mediates growth hormone negative feedback by effects on both the hypothalamus and the pituitary. *Science.* 1981 Jun 12;**212**(4500):1279–1281. [[PubMed](#)]
- Thorner MO, Rivier J, Spiess J, Borges JL, Vance ML, Bloom SR, Rogol AD, Cronin MJ, Kaiser DL, Evans WS, et al. Human pancreatic growth-hormone-releasing factor selectively stimulates growth-hormone secretion in man. *Lancet.* 1983 Jan 1;**1**(8314-5):24–28. [[PubMed](#)]

- Wehrenberg WB, Brazeau P, Luben R, Böhlen P, Guillemin R. Inhibition of the pulsatile secretion of growth hormone by monoclonal antibodies to the hypothalamic growth hormone releasing factor (GRF). *Endocrinology*. 1982 Dec;**111**(6):2147–2148. [[PubMed](#)]
- Furlanetto RW, Underwood LE, Van Wyk JJ, D'Ercole AJ. Estimation of somatomedin-C levels in normals and patients with pituitary disease by radioimmunoassay. *J Clin Invest*. 1977 Sep;**60**(3):648–657. [[PMC free article](#)] [[PubMed](#)]
- Lloyd B, Burrin J, Smythe P, Alberti KG. Enzymic fluorometric continuous-flow assays for blood glucose, lactate, pyruvate, alanine, glycerol, and 3-hydroxybutyrate. *Clin Chem*. 1978 Oct;**24**(10):1724–1729. [[PubMed](#)]
- Veldhuis JD, Johnson ML. Cluster analysis: a simple, versatile, and robust algorithm for endocrine pulse detection. *Am J Physiol*. 1986 Apr;**250**(4 Pt 1):E486–E493. [[PubMed](#)]
- Evans WS, Faria AC, Christiansen E, Ho KY, Weiss J, Rogol AD, Johnson ML, Blizzard RM, Veldhuis JD, Thorner MO. Impact of intensive venous sampling on characterization of pulsatile GH release. *Am J Physiol*. 1987 Apr;**252**(4 Pt 1):E549–E556. [[PubMed](#)]
- Mauras N, Blizzard RM, Link K, Johnson ML, Rogol AD, Veldhuis JD. Augmentation of growth hormone secretion during puberty: evidence for a pulse amplitude-modulated phenomenon. *J Clin Endocrinol Metab*. 1987 Mar;**64**(3):596–601. [[PubMed](#)]
- Steiner RA, Stewart JK, Barber J, Koerker D, Goodner CJ, Brown A, Illner P, Gale CC. Somatostatin: a physiological role in the regulation of growth hormone secretion in the adolescent male baboon. *Endocrinology*. 1978 May;**102**(5):1587–1594. [[PubMed](#)]
- DEMENT W, KLEITMAN N. Cyclic variations in EEG during sleep and their relation to eye movements, body motility, and dreaming. *Electroencephalogr Clin Neurophysiol*. 1957 Nov;**9**(4):673–690. [[PubMed](#)]
- FISHER C, GORSS J, ZUCH J. CYCLE OF PENILE ERECTION SYNCHRONOUS WITH DREAMING (REM) SLEEP. PRELIMINARY REPORT. *Arch Gen Psychiatry*. 1965 Jan;**12**:29–45. [[PubMed](#)]
- Coccagna G, Mantovani M, Brignani F, Manzini A, Lugaresi E. Laboratory note. Arterial pressure changes during spontaneous sleep in man. *Electroencephalogr Clin Neurophysiol*. 1971 Sep;**31**(3):277–281. [[PubMed](#)]
- Orr WC, Hoffman HJ, Hegge FW. Ultradian rhythms in extended performance. *Aerosp Med*. 1974 Sep;**45**(9):995–1000. [[PubMed](#)]
- Oswald I, Merrington J, Lewis H. Cyclical "on demand" oral intake by adults. *Nature*. 1970 Mar 7;**225**(5236):959–960. [[PubMed](#)]
- Levin BE, Rappaport M, Natelson BH. Ultradian variations of plasma noradrenaline in humans. *Life Sci*. 1979 Aug 13;**25**(7):621–627. [[PubMed](#)]
- Tannenbaum GS, Martin JB, Colle E. Ultradian growth hormone rhythm in the rat: effects of feeding, hyperglycemia, and insulin-induced hypoglycemia. *Endocrinology*. 1976 Sep;**99**(3):720–727. [[PubMed](#)]
- Tannenbaum GS, Rorstad O, Brazeau P. Effects of prolonged food deprivation on the ultradian growth hormone rhythm and immunoreactive somatostatin tissue levels in the rat. *Endocrinology*. 1979 Jun;**104**(6):1733–1738. [[PubMed](#)]
- Tannenbaum GS. Growth hormone secretory dynamics in streptozotocin diabetes: evidence of a role for endogenous circulating somatostatin. *Endocrinology*. 1981 Jan;**108**(1):76–82. [[PubMed](#)]
- Cahill GF, Jr, Herrera MG, Morgan AP, Soeldner JS, Steinke J, Levy PL, Reichard GA, Jr, Kipnis DM. Hormone-fuel interrelationships during fasting. *J Clin Invest*. 1966 Nov;**45**(11):1751–1769. [[PMC free article](#)] [[PubMed](#)]
- Bougneres PF, Artavia-Loria E, Ferre P, Chaussain JL, Job JC. Effects of hypopituitarism and growth hormone replacement therapy on the production and utilization of glucose in childhood. *J Clin Endocrinol Metab*. 1985 Dec;**61**(6):1152–1157. [[PubMed](#)]
- Bratusch-Marrain PR, Smith D, DeFronzo RA. The effect of growth hormone on glucose metabolism and insulin secretion in man. *J Clin Endocrinol Metab*. 1982 Nov;**55**(5):973–982. [[PubMed](#)]
- Felig P, Marliss EB, Cahill GF, Jr. Metabolic response to human growth hormone during prolonged starvation. *J Clin Invest*. 1971 Feb;**50**(2):411–421. [[PMC free article](#)] [[PubMed](#)]
- Fain JN, Kovacev VP, Scow RO. Effect of growth hormone and dexamethasone on lipolysis and metabolism in isolated fat cells of the rat. *J Biol Chem*. 1965 Sep;**240**(9):3522–3529. [[PubMed](#)]
- Haymond MW, Karl I, Weldon VV, Pagliara AS. The role of growth hormone and cortisone on glucose and gluconeogenic substrate regulation in fasted hypopituitary children. *J Clin Endocrinol Metab*. 1976 May;**42**(5):846–856. [[PubMed](#)]
- Merimee TJ, Felig P, Marliss E, Fineberg SE, Cahill GG, Jr. Glucose and lipid homeostasis in the absence of human growth hormone. *J Clin Invest*. 1971 Mar;**50**(3):574–582. [[PMC free article](#)] [[PubMed](#)]

- Owen OE, Felig P, Morgan AP, Wahren J, Cahill GF., Jr Liver and kidney metabolism during prolonged starvation. *J Clin Invest.* 1969 Mar;**48**(3):574–583. [[PMC free article](#)] [[PubMed](#)]
- Manson JM, Wilmore DW. Positive nitrogen balance with human growth hormone and hypocaloric intravenous feeding. *Surgery.* 1986 Aug;**100**(2):188–197. [[PubMed](#)]
- Imaki T, Shibasaki T, Shizume K, Masuda A, Hotta M, Kiyosawa Y, Jibiki K, Demura H, Tsushima T, Ling N. The effect of free fatty acids on growth hormone (GH)-releasing hormone-mediated GH secretion in man. *J Clin Endocrinol Metab.* 1985 Feb;**60**(2):290–293. [[PubMed](#)]

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