INSULIN-LIKE GROWTH FACTOR I IN DRIED BLOOD SPOT

What is IGF-1?

IGF-1, also known as Somatomedin C, is a polypeptide hormone similar in structure to insulin and primarily produced in the liver. It is one of the main mediators of the actions of growth hormone in promoting muscular and skeletal growth. IGF-1 is itself a powerful anabolic hormone, and it also prevents premature cell death by inhibiting apoptosis. Because of its similarity to insulin, it also weakly activates the insulin receptor and therefore has insulin-like effects when present in large quantities. Circulating IGF-1 is almost 100% bound to IGF binding proteins (IGFBP), the most abundant of these being IGFBP-3. These binding proteins stabilize IGF-1, prolonging its half-life in the bloodstream. Blood levels of IGF-1 are low in young children, peaking during the pubertal growth spurt and then declining steadily with age. IGF-1 is stable in whole blood dried on filter paper and therefore can be conveniently and accurately measured in dried blood spots[1].

Why Test IGF-1?

Growth hormone (GH) excess or deficiency

Growth hormone (GH) stimulates IGF-1 production in the liver, and therefore IGF-1 levels reflect average daily levels of GH[2]. Unlike GH, levels of IGF-1 do not fluctuate throughout the day. Other hormones affecting IGF-1 levels include thyroxine, cortisol and sex steroids[3]. The steady decline in GH production with increasing age, subsequent to the pubertal growth spurt, tends to be associated with an age-dependent decrease in IGF-1 levels. IGF-1 testing can be useful for patients with symptoms of premature aging associated with adult GH deficiency. It is particularly important to test for IGF-1 whenever GH supplementation is being used to treat premature aging or to improve wellbeing, so that levels are kept within the expected physiological range[4,5].

Nutritional status

Liver production of IGF-1 is affected by nutritional factors, including protein deficiency and low insulin levels. Because of this, IGF-1 is a sensitive indicator of nutritional status, and a more useful marker than pre-albumin, retinol-binding protein or transferrin for monitoring patients with eating disorders[6,7]. A large study[8] demonstrated that in underweight and normal weight individuals, IGF-1 levels increase as BMI increases. However, in obese individuals, particularly those with visceral adiposity, IGF-1 levels decrease as BMI increases.

Skeletal maturity

Important new research using the ZRT IGF-1 dried blood spot test has demonstrated its application for assessing a young individual's cervical skeletal maturation stage[9]. Until now, peak mandibular bone growth has been assessed on a largely subjective basis using inconvenient and expensive radiography, resulting in radiation exposure. With IGF-1 testing in blood spot, dentists can safely assess a patient's cervical stage to determine whether a patient has attained or passed the peak pubertal growth, and therefore time orthodontic and other procedures more optimally.

Cancer

Because of its mitogenic and anti-apoptotic actions, IGF-1 has been implicated in carcinogenesis. High IGF-1 levels have been linked with several types of cancer, including prostate, premenopausal breast, colorectal and lung cancer[10]. However, meta-analyses show that these associations are modest and variable between research groups[11,12] and may be influenced by the effects of nutritional factors and BMI on IGF-1 levels[13]. Recent research has shown that estrogen acts synergistically with IGF-1 to enhance breast cancer cell growth in vitro[14]. Little is known about these relationships in vivo or if inhibitors of IGF-1 would benefit breast cancer patients[15].

866.600.1636 | info@zrtlab.com | zrtlab.com

Revised 02.25.14

ZRT LABORATORY

Dried Blood Spot Testing.
Minimally-invasive home test kit.

Cardiovascular Disease

The visceral obesity and related metabolic disturbances that contribute significantly to cardiovascular disease and diabetes risk is frequently a result of neuroendocrine dysregulation, characterized by hormonal imbalances such as increased cortisol levels and suppressed GH secretion[16]. The generally lower IGF-1 levels associated with increasing obesity[8] may be partly a reflection of reduced GH production. Indeed, GH therapy has been used, with promising results, to treat patients with visceral obesity in an attempt to correct endocrine abnormalities and reduce cardiometabolic risk[17]. While these therapies are not yet widely accepted, it is important to monitor GH supplementation by ensuring that IGF-1 levels stay within the physiological range[5].

In addition, it is emerging that low IGF-1 levels are also more directly involved in the pathogenesis of insulin resistance, metabolic syndrome, type II diabetes, and cardiovascular disease[18]. The anabolic role of IGF-1 is mediated by its involvement in increasing insulin sensitivity and peripheral glucose uptake; low IGF-1 levels are associated with poorer blood sugar control and worse cardiovascular outcomes in diabetics[19]. Increased muscle mass as a result of resistance exercise in sedentary postmenopausal women has been found to be linked with significantly higher IGF-1 levels[20,21], which may contribute to the cardiometabolic benefits of resistance training.

IGF-1 is now known to have a critical role in vascular protection[18,22]. This is primarily mediated by IGF-1's role in increasing nitric oxide bioavailability in the vascular endothelium[18,23,24], low IGF-1 levels are therefore thought to reduce vascular protection. Measurement of IGF-1 is now suggested as an important additional marker of cardiovascular disease risk[24].

Advantages of a Simple Dried Blood Spot Test

- A simple finger stick provides the few drops of blood required, which are collected on the filter paper provided
- Convenient sample collection at home – no phlebotomist required
- Easy shipment of samples by regular mail – samples are stable for up to a month at room temperature
- Dried bloodspots carry minimal infection risk – infectious agents such as HIV are inactivated in dried blood
- Excellent correlation with serum/plasma IGF-1 levels

Clinical Utility

- IGF-1 levels are an indicator of growth hormone secretion; low values imply growth hormone deficiency and high values are seen in acromegaly or gigantism
- Low IGF-1 levels are seen in malnutrition or anorexia, and IGF-1 can be used as a sensitive indicator to monitor nutritional repletion
- Dentists can use IGF-1 levels to assess cervical stage of patients, predict residual facial skeletal growth, and thus properly time orthodontic procedures
- In growth hormone supplementation, IGF-1 levels should be kept within the physiological range to ensure safe dosing levels
- IGF-1 can be used as an adjunct to cardiometabolic risk testing with ZRT's CardioMetabolic Profile; low IGF-1 levels are associated with increased risk of cardiovascular disease, especially in individuals with diabetes

References

1. Diamandi A, Khosravi MJ, Mistry J, Martinez V, Guevara-Aguirre J. Filter paper blood spot assay of human insulin-like growth factor I (IGF-I) and IGF-binding protein-3 and preliminary application in the evaluation of growth hormone status. J Clin Endocrinol Metab. 1998;83(7):2296-301.
2. Clemmons DR. Commercial assays available for insulin-like growth factor I and their use in diagnosing growth hormone deficiency. Horm Res. 2001;55 Suppl 2:73-9.
3. Clemmons DR. Clinical utility of measurements of insulin-like growth factor 1. Nat Clin Pract Endocrinol Metab. 2006;2(8):436-46.
4. Schwartz ET, Holtorf K. Hormones in wellness and disease prevention: common practices, current state of the evidence, and questions for the future. Prim Care. 2008;35(4):669-705.
5. Higham CE, Jostel A, Trainer PJ. IGF-I measurements in the monitoring of GH therapy. Pituitary. 2007;10(2):159-63.
6. Swenne I, Stridsberg M, Thurfjell B, Rosling A. Insulin-like growth factor-1 as an indicator of nutrition during treatment of adolescent girls with eating disorders. Acta Paediatr. 2007;96(8):1203-8.
7. Caregaro L, Favaro A, Santonastaso P, Alberino F, Di Pascoli L, Nardi M, Favaro S, Gatta A. Insulin-like growth factor 1 (IGF-1), a nutritional marker in patients with eating disorders. Clin Nutr. 2001;20(3):251-7.
8. Schneider HJ, Saller B, Klotsche J, März W, Erwa W, Wittchen HU, Stalla GK. Opposite associations of age-dependent insulin-like growth factor-I standard deviation scores with nutritional state in normal weight and obese subjects. Eur J Endocrinol. 2006;154(5):699-706.
9. Masoud M, Masoud I, Kent RL Jr, Gowharji N, Cohen LE. Assessing skeletal maturity by using blood spot insulin-like growth factor I (IGF-I) testing. Am J Orthod Dentofacial Orthop. 2008;134(2):209-16.
10. Giovannucci E. Insulin-like growth factor-I and binding protein-3 and risk of cancer. Horm Res. 1999;51 Suppl 3:34-41.
11. Renehan AG, Zwahlen M, Minder C, O'Dwyer ST, Shalet SM, Egger M. Insulin-like growth factor (IGF)-I, IGF binding protein-3, and cancer risk: systematic review and meta-regression analysis. Lancet. 2004;363(9418):1346-53.
12. Renehan AG, Harvie M, Howell A. Insulin-like growth factor (IGF)-I, IGF binding protein-3, and breast cancer risk: eight years on. Endocr Relat Cancer. 2006;13(2):273-8.
13. Giovannucci E, Pollak M, Liu Y, Platz EA, Majeed N, Rimm EB, Willett WC. Nutritional predictors of insulin-like growth factor I and their relationships to cancer in men. Cancer Epidemiol Biomarkers Prev. 2003;12(2):84-9.
14. Dupont J, Le Roith D. Insulin-like growth factor 1 and oestradiol promote cell proliferation of MCF-7 breast cancer cells: new insights into their synergistic effects. Mol Pathol. 2001;54(3):149-54.
15. Kleinberg DL, Wood TL, Furth PA, Lee AV. Growth hormone and insulin-like growth factor-I in the transition from normal mammary development to preneoplastic mammary lesions. Endocr Rev. 2009;30(1):51-74.
16. Franco C, Bengtsson BA, Johannsson G. Visceral obesity and the role of the somatotropic axis in the development of metabolic complications. Growth Horm IGF Res. 2001;11 Suppl A:S97-102.
17. Johannsson G, Bengtsson BA. Growth hormone and the metabolic syndrome. J Endocrinol Invest. 1999;22(5 Suppl):41-6.
18. Ezzat VA, Duncan ER, Wheatcroft SB, Kearney MT. The role of IGF-I and its binding proteins in the development of type 2 diabetes and cardiovascular disease. Diabetes Obes Metab. 2008;10(3):198-211.
19. Janssen JA, Lamberts SW. The role of IGF-I in the development of cardiovascular disease in type 2 diabetes mellitus: is prevention possible? Eur J Endocrinol. 2002;146(4):467-77.
20. Vale RG, de Oliveira RD, Pernambuco CS, de Meneses YP, Novaes JD, de Andrade AD. Effects of muscle strength and aerobic training on basal serum levels of IGF-1 and cortisol in elderly women. Arch Gerontol Geriatr. 2009, 49(3): 343-7.
21. Orsatti FL, Nahas EA, Maesta N, Nahas-Neto J, Burini RC. Plasma hormones, muscle mass and strength in resistance-trained postmenopausal women. Maturitas. 2008;59(4):394-404.
22. Abbas A, Grant PJ, Kearney MT. Role of IGF-1 in glucose regulation and cardiovascular disease. Expert Rev Cardiovasc Ther. 2008;6(8):1135-49.
23. Thum T, Fleissner F, Klink I, Tsikas D, Jakob M, Bauersachs J, Stichtenoth DO. Growth hormone treatment improves markers of systemic nitric oxide bioavailability via insulin-like growth factor-I. J Clin Endocrinol Metab. 2007;92(11):4172-9.
24. Conti E, Carrozza C, Capoluongo E, Volpe M, Crea F, Zuppi C, Andreotti F. Insulin-like growth factor-1 as a vascular protective factor. Circulation. 2004;110(15):2260-5