PROJECT SUMMARY

"GH-2004; The development of a Methodology for Detectiong Abuse with Growth Hormone in Sport"

P. Sönksen, R. Holt (The School of Medicine, University of Southampton, Southampton, UK), **D. Cowan** (Drug Control Centre, King's College London, UK), **E. Bassett** (University of Kent, Canterbury, UK)

Growth hormone (GH) is a naturally occurring hormone produced by the pituitary gland, which has strong growth-promoting properties regulating muscle and fat tissue and is widely accepted as being a major drug of abuse in sport. Its use is banned under the International Olympic Committee (IOC) and World Anti Doping Agency (WADA) list of prohibited substances. The detection of doping with GH poses a formidable challenge, as it is identical to that which is produced naturally in the body.

The concentrations of GH vary in the blood during the course of the day as under normal circumstances, it is secreted by the pituitary gland in short bursts, each lasting a few minutes. Exercise and stress are powerful stimuli for GH secretion.

The methods for detecting the abuse of androgenic anabolic steroids and related substances measured by mass spectroscopy are highly sophisticated but no such methods have been developed for testing for abuse with hormones such as GH and insulin-like growth factor-I (IGF-I). Immuno-assays and blood sampling are required for the detection of these substances and because the hormones are rapidly degraded in the body, urine analyses are not an option. Although it has been shown that it is possible to detect recombinant human growth hormone (rhGH) in blood, such tests have yet to be properly validated and are only able to detect rhGH within a short 'window of opportunity' of <24 hours after the last injection of rhGH. Furthermore they will not detect any injection of pituitary-derived GH that is readily available.

GH-2000 was a research project funded jointly by the European Union (EU) and the IOC. Its aim was to develop a method for the detection of GH abuse. It reported its findings to the EU and the IOC in January 1999. The GH-2000 project has shown that a test for GH using GH-dependent markers of GH action is feasible and scientifically valid.

The Development of Methodology for Detecting Growth Hormone in Sport: GH2004

Results and Conclusions

- It is believed that growth hormone (GH) is abused by athletes and other professional sports men and women.
- The use of GH is banned under the World Anti-Doping Agency (WADA) list of prohibited substances.
- The detection of abuse with GH by poses several challenges because injectable GH is identical to naturally produced GH.
- The GH-2000 study based at St Thomas' Hospital, London and led by Professor Peter Sönksen showed that it is possible to detect GH abuse by measuring insulin like growth factor –I (IGF-I) and type 3 procollagen (P-III-P) whose concentrations increase in response to injections of GH and the application of discriminant function analysis.
- The results of GH-2000 were presented to a panel of international experts at an IOC-organised Workshop in Rome in April 1999. This review raised a number of key issues that needed addressing before any test could be implemented. The main issue concerned possible ethnic effects on the proposed markers, since the majority of volunteers in GH-2000 were white European.
- The GH-2004 project, which is a 3-year project based at the University of Southampton, is funded by WADA and the US Anti-Doping Agency and aims to address these concerns.
- The first part of the project, which was funded by WADA, measured serum IGF-I and P-III-P in blood samples obtained from 242 male and 62 female elite athletes from different ethnic backgrounds within 2 hours of the end of competition at 9 international sporting events in 13 disciplines.
- The study showed that although there are small differences (<20%) in the concentrations of IGF-I and P-III-P between different ethnic groups, the majority of values for individuals of non-white European background lie within the normal range for the white European subjects.
- Application of the GH-2000 discriminant function analysis formulae to the GH-2004 subjects showed that no individual would have been falsely accused of doping.
- The significance of these results means that the test can be applied across different ethnicities. As it is extraordinarily difficult to define ethnicity, if there had been major differences between ethnic groups, it would have been impossible to apply the test.

Publications

McHugh CM, Park RT, Sonksen PH, Holt RI. Challenges in detecting the abuse of growth hormone in sport. Clin Chem. 2005 Sep; 51(9):1587-93. Epub 2005 Jul 14.

McHugh C, Holt RIG. (2003) Growth Hormone in Sport. Science and Public Affairs. Dec. 18-19

Conference Presentations

GH-2004 project. An update World Anti-Doping Agency Consensus Meeting Lausanne 2003

Anabolic therapies: what can we learn from sports doping? Cachexia, Berlin 2003

The challenges of detecting growth hormone abuse in sport: an overview. US Anti-Doping Agency Symposium on Doping with Growth Hormone in Sport Dallas 2004

GH-2000 project: an overview. US Anti-Doping Agency Symposium on Doping with Growth Hormone in Sport Dallas 2004

GH-2004 project: The affects of ethnicity on GH-dependent markers. US Anti-Doping Agency Symposium on Doping with Growth Hormone in Sport Dallas 2004

The challenges of detecting GH abuse in sport. Tunisian College of Sports Medicine. Tunis 2004

The challenges of detecting GH abuse in sport. 9th Annual Congress of the European College of Sport Science, Clermont-Ferrand 2004

The challenges of detecting growth hormone abuse in sport: Results of the cross-sectional study. Presentation to Mr Richard Caborn Minister for Sport. Southampton 2005

The challenges of detecting GH abuse in sport. Real Madrid Foundation International Symposium on doping in Sport. Madrid.