The pharmaceutical industry in anti-doping: Possibilities and limitations
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Possibilities and limitations

Possibilities

- Inform about
  - The molecules
  - Secretion and physiology
  - Potential analysis

- To prevent misuse of pharmaceutical products companies can participate/support international projects to develop tests that can detect misuse of the products

Limitations

- Prescribed medications
- Sponsorships
Biosynthetic hGH molecule

- Growth hormone (GH) – is single chain polypeptide with 191 amino acids and two S-S bridges – 22Kd
- Identical to the hGH produced by the pituitary gland at the basis of the brain
Role of Growth Hormone

- Regulates growth in children
- Plays significant role in multitude of metabolic functions
  - GH is more than cm
- Produced throughout life; necessary after adult height reached
- GH deficiency causes deleterious effects in children and adults

Growth Hormone Physiology

Hypothalamus

GHRH

Somatostatin

GH

IGF-I

Hypothalamus

GHRH

Somatostatin

GH

IGF-I

Growth Hormone Physiology

Hypothalamus

GHRH

Somatostatin

GH

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Hypothalamus

GHRH

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GH

IGF-I
GH secretion is age-dependent

Graph showing GH secretion rate (mg/24h) over years.
Our aspiration is to improve life for patients where GH will make a clinically relevant difference

• GH should only be used for treatment of diseases for which it is indicated and when prescribed by a medical doctor.
  • Adults with GH deficiency
  • Children with GH deficiency
  • Short children born small for gestational age (SGA)
What’s adult GH deficiency (AGHD)?

Characteristics of AGHD

- Abnormal body composition
  - ↑ fat mass, ↓ muscle mass
- Increased risk of CVD
  - ↑ total cholesterol & LDL, ↓ HDL
- Impaired quality of life

AGHD patient

- Before GH treatment
- After 6 months on GH

Reduced visceral and sc. fat
Effect of GH in AGHD - Body composition

Hansen et al. 1995

Fat mass and Lean body mass changes (%)

Placebo vs GH comparison for different body parts:
- Total
- Head/neck
- Arm
- Trunk
- Leg

Hansen et al. 1995
Effect of GH in AGHD

Exercise capacity ↑
What is SGA?

- Small for gestational age (SGA):
  - A baby born shorter and/or lighter than normal for its gestational age.

- Definition:
  - Birth length and/or birth weight < −2 SDS

- Approximately 5% of infants are born SGA
  - Most catch-up and normalise their height before 2 years of age
  - But approx. 10% remain short (height SDS<−2) throughout childhood
Can GH be measured

**Yes!**
**In blood not in urine**

**Direct method**
- 22K/20K ratio method to detect GH abuse during GH administration
  - The window of detection following withdrawal of GH is short, max 36 hours.
    - Pituitary gland produce a mixture of 22Kd and 20Kd & 17Kd, ratio approx 80:20
    - bhGH is 100% 22Kd

**Indirect methods**
- GH dependent variables
  - IGF-I, IGFBP-3, ALS
  - Bone and soft tissue markers, osteocalcin, PICP, ICTP, P-III-P
- Normative values in athletes in men, women and all races
- Algorithm based IGF-I, IGFBPs and bone parameters
Novo Nordisk collaboration with IOC and EU

- **1996-2001**
  - **GH 2000 – developing a test for GH misuse**
    - Study performed by 4 European Universities in the period 1996 - 2001
      - Key investigators: Peter Sönksen, London, UK - Jens Sandahl Christiansen, Aarhus, Denmark – Bengt-Åke Bengtsson, Gothenburg, Sweden and S Longobardi, Naples, Italy
    - Sponsors: IOC, EU, **Novo Nordisk** & Pfizer
    - Results published in peer reviewed journals in the period 2003-2006
Novo Nordisk collaboration WADA, Australian and Japanese Institutes of Sports Sciences I

2003 on-going to 2008

- Defining interactions between testosterone and GH: developing a robust test for GH doping
  - Key investigator: Ken Ho, Sydney, Australia
  - Sponsors: Australian & Japanese Anti-doping Agencies and Novo Nordisk
  - Published at the Endocrine Society meeting in the US
Novo Nordisk collaboration WADA, Australian and Japanese Institutes of Sports Sciences II

Study to detect misuse of GH & testosterone (T)

- 8-week study in 97 (33F/64M) non-competition athletes, aged 18-40 years – GH 2mg/day, T 250 g/week
  - Women assigned to GH or placebo
  - Men assigned to GH, T, a combination of these, or placebo
  - Samples before, during and 6 weeks after stopping drugs
    - T has a greater protein and cellular anabolic effect than GH
    - GH or T supplementation in the doses used does not significantly improve physical performance, while combined treatment enhance anaerobic work capacity in men
The **power of the mind** in a double-blind placebo controlled study
- The athletes in the placebo group who believed they were on GH not only had a perceived improvement on performance but also in measured physical improvement.
- The effect was greater in men.

**Method to detect GH abuse:** The 22K/20K ratio useful method for detecting GH abuse during GH administration.
- The window of detection following withdrawal of GH is short, max 36 hours.
GH prescribed medication

- GH must be prescribed by a physician
- Abuse of GH can have side effects
- It is known that healthy young and elderly people take GH supplementation to boost performance and energy levels
  - The risk and costs outweigh potential benefits
  - The Australian study used high, but safe doses of GH and found that GH had no beneficial effects!
Novo Nordisk position on Norditropin and doping

- **Norditropin®** should only be used to improve life for patients where GH will make a clinically relevant difference and when prescribed by a medical doctor.

- Novo Nordisk strongly advises against any use of Norditropin as a performance enhancement drug by athletes or bodybuilders: It’s effect is questionable and the long term side effects of such use are unknown and could be serious.

- To help prevent misuse of GH, Novo Nordisk participates in international projects to develop tests that can detect misuse of GH.
Thank you very much listening!

They grow and grow-up to be happy adults

Any questions