

The Results Management of AAFs involving TUEs – the contribution of medical science

WADA/CoE TUEC Chairs Symposium

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Strasbourg / December 11th 2009

World Anti-Doping Program

- **Level 1: The Code**
- **Level 2: International Standards**
- **Level 3: Models of Best Practice and Guidelines**

Article 2: Anti-Doping Rule Violations

- **2.1 Presence of a Prohibited Substance or its Metabolites or Markers in an Athlete's Sample**
- **2.2 Use or Attempted Use by an Athlete of a Prohibited Substance or Prohibited Method**

Article 10: Sanctions on Individuals

- **The period of Ineligibility imposed for a first Anti-Doping Rule Violation shall be in general two years, unless the conditions for eliminating or reducing the period of Ineligibility or the conditions for increasing the period of Ineligibility are met.**
- **For violations involving Specified Substances the period of Ineligibility shall be for a first violation at minimum, a reprimand and no period of Ineligibility from future Events, and at a maximum, two years of Ineligibility.**

Article 10: Sanctions on Individuals

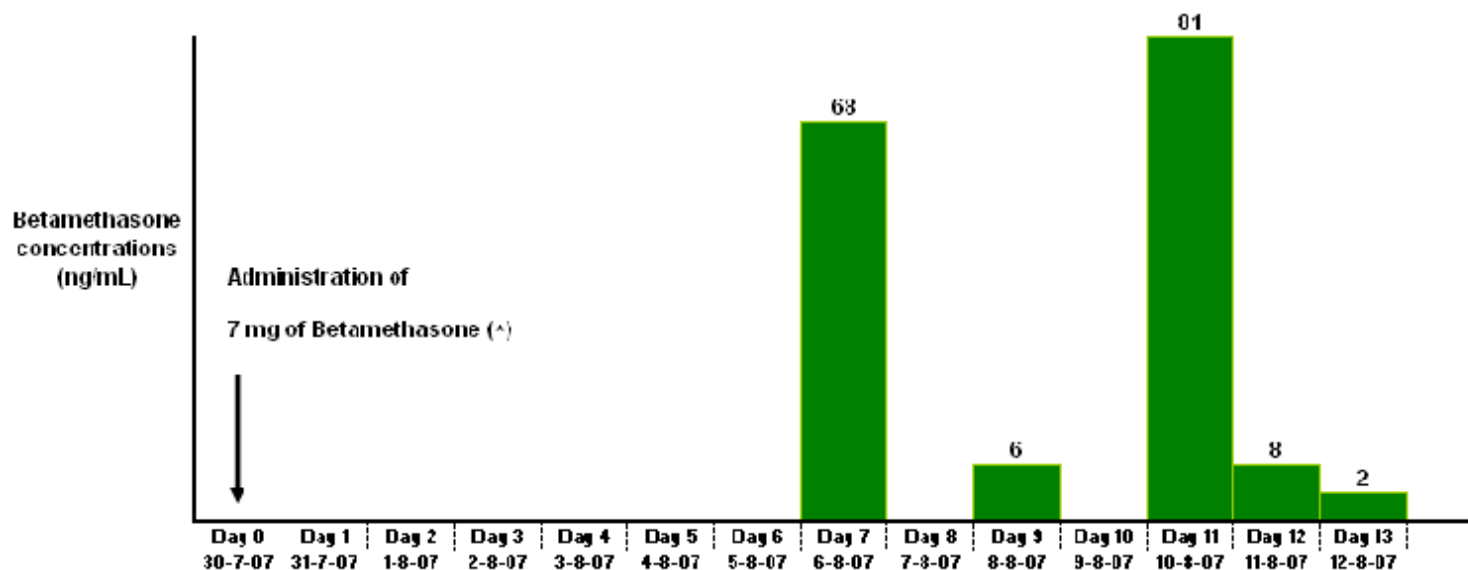
- For Multiple Violations

Second Violation \ First Violation	RS	FFMT	NSF	St	AS	TRA
RS	1-4	2-4	2-4	4-6	8-10	10-life
FFMT	1-4	4-8	4-8	6-8	10-life	life
NSF	1-4	4-8	4-8	6-8	10-life	life
St	2-4	6-8	6-8	8-life	life	life
AS	4-5	10-life	10-life	life	life	life
TRA	8-life	life	life	life	life	life

World Anti-Doping Code (revised), World Antidoping Agency 2009.

Case 1

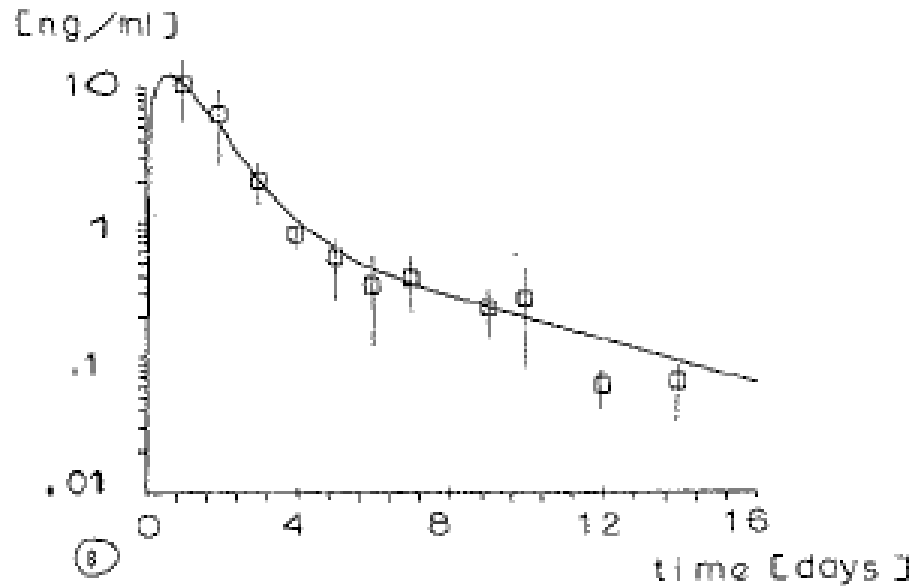
- **Cycling rider**
- **Betamethasone AAF (specified substance)**
- **Two Betamethasone AAFs during the same International Event**
- **Athlete claimed that the results were cover by an ATUE for the concerned compound**



(*) - Intra-articular acromion-clavicular administration of 7 mg of Betamethasone covered by an ATUE (CNAD 262/07)

CODE	COLLECTION DATE	SAMPLE NUMBER	LAD NUMBER	CONCENTRATION (ng/mL)
PORÉM	07-08-07	A354806	2615	68
RATEIRO	09-08-07	A355078	2620	6
REBOLAR	11-08-07	A353908	2627	81
RFCFOSO	12-08-07	A354164	2637	8
REFEITA	13-08-07	A354168	2650	2

Case 1



- **Non applicability of the Article 10.4 – Elimination or reduction of the period of ineligibility for specified substances under specific situations**

* Derendorf, H., Möllmann, H., Grüner, A., Haack, D. and Gyselby, G. **Pharmacokinetics and pharmacodynamics of glucocorticoid suspensions after intraarticular administration.** Clin Pharmacology Ther 1986; 39:313-7.

Case 2

- **Football player**
- **Methylprednisolone AAF (specified substance)**
- **Athlete and team physician claimed that the result was covered by an ATUE for Methylprednisolone, where an intra-articular administration of 20 mg of that compound was declared 38 days before the in competition test and that the fact of a previous surgery on that joint could explain the delay in the urinary excretion. The delay could be explained to a chronic inflammation of the synovial membrane after surgery.**
- **The estimated urinary concentration of Methylprednisolone was 40.5 ng/mL**

Case 2

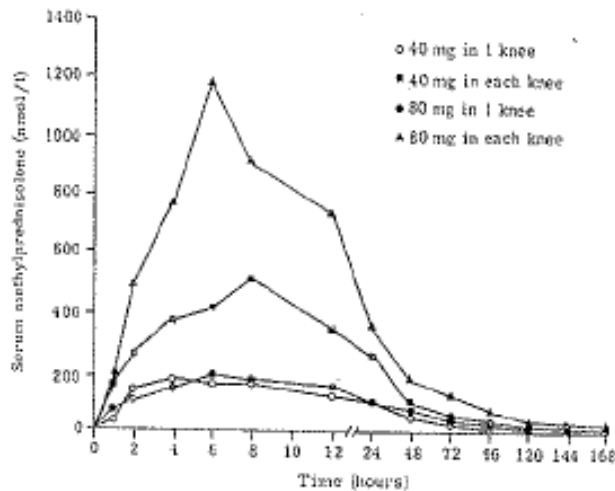


Fig. 1 Mean serum methylprednisolone levels following intra-articular injections of methylprednisolone acetate.

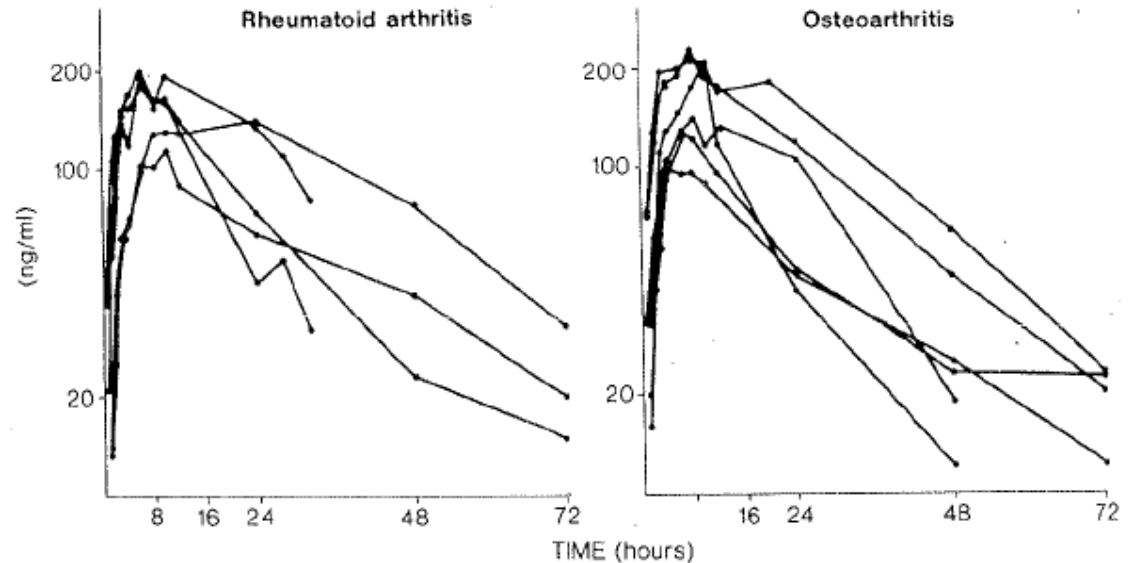


Figure 1: Plasma-concentration time profiles in RA and OA patients following intra-articular injection of 80 mg methylprednisolone (depot-medrol; Upjohn) into the knee.

Non applicability of the Article 10.4 – Elimination or reduction of the period of ineligibility for specified substances under specific situations

* Armstrong, R.D. English, J. Gibson, J., Chakraborty, J. Marks, V. Serum methylprednisolone levels following intra-articular injection of methylprednisolone acetate. Annals of the Rheumatic Diseases, 1981, 40, 571-574.

** Bertouch, J.V. Sallustio, B.C. Meffin, P.J. Brooks, P.M. A comparison of plasma methylprednisolone concentrations following intra-articular injection in patients with rheumatoid arthritis and osteoarthritis. Aust NZ J Med 1983; 13:583-586.

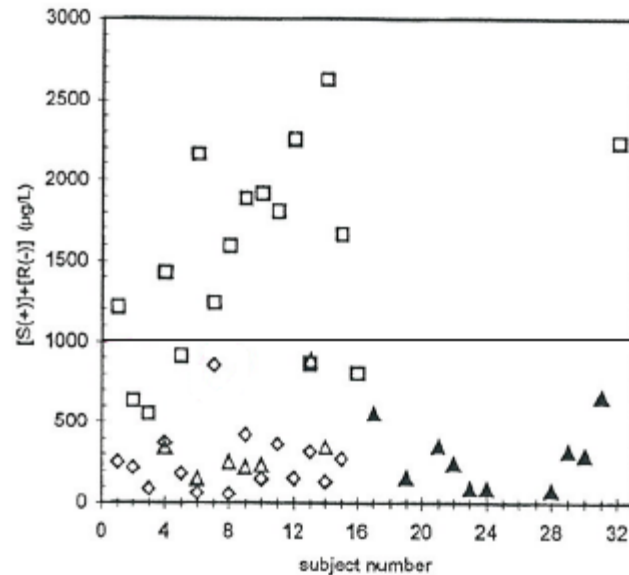
- **9.2 Na *Athlete's* failure to declare *Use* on a *Doping Control Form* and through *ADAMS* when available, as stated in Article 9.1, shall not be na anti-doping rule violation.**

[Comment to 9.2: The rules of Anti-Doping Organizations with jurisdiction over an Athlete may impose consequences other than an anti-doping rule violation for failure to declare.]

Case 3

- **Football player**
- **3 Salbutamol AAFs (Beta2 Agonist - specified substance). Athlete and team physician claimed that the result was covered by an ATUE for inhaled salbutamol for treatment of asthma (threshold of 1000ng/mL)**
- **The urinary concentrations of salbutamol were 2400 ng/mL, 2100 ng/mL and 1900 ng/mL in the three samples**

- **Unannounced complementary examinations:**
 - **First urine sample collected before a training session followed by the administration of a therapeutic dosage of salbutamol by inhalation;**
 - **Second urine sample collected just after the end of the training session;**
 - **Result - The urinary concentration in the second sample of salbutamol was 750ng/mL**



Oral administration: 4 mg every 6 h over 24 h. Inhaled administration: 2 × 100 µg for study 1; 16 × 100 µg over 24 h for study 2. □, oral, nonasthmatic; △, inhaled, nonasthmatic (study 1); ▲, inhaled asthmatic; ◇, inhaled, nonasthmatic (study 2).

Non applicability of the Article 10.4 – Elimination or reduction of the period of ineligibility for specified substances under specific situation

* Bergés R. Segura J. Ventura R. Fitch K.D. Morton A.R. Farré M. Marti M. De la Torre X. Discrimination of prohibited oral use of salbutamol from authorized inhaled asthma treatment. *Clinical Chemistry*. 2000: 1365-1375

- **8.12 The substance or method, dose, frequency, route and duration of administration of the otherwise *Prohibited Substance or Prohibited Method* in question shall be specified. In case of change, a new application shall be submitted.**

Prohibited List 2010

- **S3. BETA-2 AGONISTS**

All beta-2 agonists (including both optical isomers where relevant) are prohibited except salbutamol (maximum 1600 micrograms over 24 hours) and salmeterol by inhalation which require a declaration of *Use* in accordance with the International Standard for Therapeutic Use Exemptions.

- **S3. BETA-2 AGONISTS**

The presence of salbutamol in urine in excess of 1000 ng/mL is presumed not to be an intended therapeutic use of the substance and will be considered as na *Adverse Analytical Finding* unless the *Athlete* proves, through a controlled pharmacokinetic study, that the abnormal result was the consequence of the use of a therapeutic dose (maximum 1600 micrograms over 24 hours) of inhaled salbutamol.

New version of the Code

More Proportionality

More Flexibility