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Interview with **Dr Andrew Kicman** of **King's College London** conducted by **Robert Dunn** of the **Future Leaders in Innovation Group, Viapath.**

- *How did you choose your field of expertise? Is it something that you were always interested in?*

  I was always interested in the Life Sciences and for my third year BSc project, toxicology came to the fore, as I chose to review the major findings on the pharmacological actions of the opiates and whether or not these findings linked with the treatment of heroin addicts. Upon graduation, I was offered an analytical post at St Thomas's Hospital in London, under Professor Raymond Brooks, who had introduced the screens for anabolic steroids for drug testing sport.

  I obtained a PhD, in line with my research work there, concerning analytical and biochemical aspects of androgens, in between routine analysis of sports' samples. After ten years, I then moved to the Drug Control Centre at King's College London, the sole World Anti-Doping Accredited (WADA) laboratory within the UK.

- *What motivates you in your career?*

  I have always had a passion for research and writing papers, but also I enjoy teaching. I am pleased to have launched an MSc in Analytical Toxicology at King's in 2009, which is now running in its 6th year. The last ten years have been a fresh challenge and fascinating, as I diversified into research concerning mainstream toxicology, such as the disposition of ketamine and cocaine.

- *Do you see drugs in sport as a continual arms race with testing always playing catch-up to new substances?*

  No, I do not think it is playing catch-up. There are always new substances to deal with, but often laboratories are anticipating what these substances may be and developing analytical approaches to detect their administration. The fight against doping has been also facilitated by research funding from WADA and the USA Partnership for Clean Competition.

  Examples of developing drug tests well in advance of a potential problem concerns the targeting of the selective androgen receptor modulators

(SARMs) and the exogenous insulins, both excellent pieces of work led by Mario Thevis, the Director of the Centre for Preventive Doping Research at the Sport University in Cologne.

Even so, in terms of drugs that promote skeletal muscle growth and strength, none seems to have superseded the anabolic steroids, most probably because of the combination that they are effective, inexpensive and easy to obtain.

WADA accredited laboratories are also well on top of monitoring the plethora of supplements that contain steroid analogues. There are still some analytical challenges left in detecting the administration of the anabolic steroid testosterone, particularly if it is co-administered with epitestosterone, a problem that we anticipated as far back as the1980s.

- *How soon can a substance be added to the banned list from the beginning of development of an assay for its detection?*

This can be well within a year, if the substance is a small xenobiotic molecule that can be detected by chromatography-mass spectrometry and especially if labs have a chemical standard to work with. Substances that we also produce naturally in our body can take a few years, as I well recall with my work on 5-alpha-dihydrotesterone in the 1990s.

The detection of protein hormone administration can be far more challenging, such as for EPO. An evidentially robust and sensitive test for human growth hormone administration based on the IGF-1/P-3-P approach took about 18 years and it is a credit to the tenacity of the investigators involved that they achieved their goal, with the test being effectively used at the last Olympics.

We still do not have a test for the detection of administration of human recombinant insulin, which is identical in sequence to what we produce endogenously.

- *How do you validate new assays with controls? Are controlled volunteer studies required?*

WADA accredited laboratories are also ISO17025 accredited. We follow validation guidelines, which are stringent and, I believe are of a gold standard. Controls can be urine or blood spiked with drugs (and/or their metabolites) and also from samples collected during ethically-approved drug administration studies.

- *You recently had a paper published detailing detection of significant levels of anabolic steroids in bodybuilding dietary supplements; how widespread do you think this issue is in such gym supplements?*

  There are some indications that the incidence of anabolic steroid use in the UK is similar to that of heroin or cocaine, which may or may not be the case, and that the use is nationwide. Dietary supplements containing steroids can only increase the use, as they are easily ordered through the internet.

  23 of the 24 supplements we tested contained anabolic steroids, 16 contained steroids that were different to those indicated on the packaging, including potentially hepatoxic steroids at amounts that we determined that could pose a significant risk to health.

  Teenage boys may be particularly vulnerable, as naïve users.

- *Jack3d, a stimulant previously sold as a gym supplement, was banned in 2012 following the death of a London marathon runner – do you think similar products have since taken its place? If so, what do you think is the best way to avoid such tragedies in future?*

  Yes, Pieter Cohen and his team in the USA has identified an analogue of DMAA called DMBA (1,3 dimethylbutylamine) in dietary supplements, a substance never tested in humans.

  The way to help minimise such tragedies in the future is a moot point. Law enforcement to minimise exposure to every supplement that contains a stimulant or anabolic steroid that comes onto the market is not realistic, as it takes time to include a novel drug that does not fall under the current Misuse of Drugs Act and because there are resource considerations, which means that enforcement is challenging.

  In this respect, the new psychoactive substances ('legal highs') particularly come to mind, with a dramatic increase in their availability and entrepreneurs can quickly respond to legislation by moving to a new non-controlled substance. Enforcement can be enacted in other ways, for example, the excellent strategy that the FDA is taking, writing to suppliers of gym supplements purported to fall under the USA Dietary Supplement Health and Education Act, requesting that they withdraw their product or further action will be taken.

  In addition, somehow there should be adequate and highly visible health warnings on the containers of such 'gym supplements', for example, those that contain stimulants should include a statement regarding the

general associated risks, particularly of their use in combination with exercise, that can result in cardiovascular events and death.

- *Some banned substances have been shown to be present in food, for example clenbuterol in meat; do assays always have the power to differentiate between accidental and purposeful ingestion of such substances?*

  The simple answer is no, not yet and most likely not unequivocally for a long time. This problem may become a major challenge, particularly because WADA lowered the minimum required performance level (MRPL) for clenbuterol from 2 to 0.2 ng/mL in 2013.

  WADA laboratories must be able to routinely detect and identify the presence of clenbuterol at this level, but is the detection of a trace amount of clenbuterol in an athlete's sample truly indicative that this could have only occurred due to doping? Furthermore, each generation of mass spectrometers, so far, have increased analytical sensitivity by an order of magnitude.

  Many non-drug users may be exposed to certain drugs at very low amounts, from the possibility of ingesting clenbuterol in contaminated meat (depending most likely on the country of origin of that meat) to skin contamination from contact with cocaine on bank notes.

  The consequence is that trace amounts in biological samples are now detected that would not have been detected in the past with older technology and common sense needs to prevail in interpretation of such findings.

- *Do you see techniques such as those applied to overcome the 'poppy seed defence' regarding heroin use being applied to sport doping tests as they are further refined?*

  The investigation regarding the solution to the poppy seed defence, which is published in Drug Testing and Analysis, is one that I feel very privileged to have led, but Dr Chen deserves a special mention as she undertook the project for her PhD. This work relied on chromatography-mass spectrometry and a good deal of lateral thinking.

  I have met many scientists from different WADA laboratories and the intellect these toxicologists have has left a deep impression on me. Techniques continue to be introduced and refined, helping to keep sport drug-free.

- *Do scientists involved in testing feel frustrated when positive samples are appealed, and sometimes overturned on technicalities?*

  My opinion is that as an athlete's career may be on the line, the system has to allow for such challenges and good science will always win in the end.

- *Has the exposure of drug abuse in cycling in recent years made a difference to testing in sport as a whole?*

  No doubt, more resources are going into the collection of blood samples. As an aside, credit should also be given to the US Anti-Doping Agency, who did an excellent job in investigating doping allegations concerning Lance Armstrong. I hope the ramifications are such that it has spawned a new era in cycling compared to what was before.

- *What would you want people to remember about your career after you've retired?*

  That I made a difference in academia to a number of MSc and PhD students, who are now carving their own careers in analytical toxicology. In addition, my keen support of the London Toxicology Group and the journal Drug Testing and Analysis.

- *What scientific achievement has excited you most recently?*

  Professor David Nutt and Dr Les King's publications, in that they continue to press for a fully scientifically-based UK Misuse of Drugs Act, based on drug harm.