



INTERNATIONAL
ASSOCIATION OF

THERAPEUTIC DRUG
MONITORING AND
CLINICAL TOXICOLOGY

Website: www.iatdmct.org

10th International Congress of Therapeutic Drug Monitoring & Clinical Toxicology, Nice, France, September 9-14, 2007

Young Scientists Congress Overview

Upon reflection the congress was a great success for the initiation of the Young Scientist (YS) activities within the association. YS events started on the Sunday with a relaxed lunch (kindly sponsored by Microgenics, now part of Thermo Fisher) followed by the first ever IATDMCT YS Workshop. The workshop format included three excellent oral presentations covering clinical toxicology (Frank T. Peters, YSC Chairman), therapeutic drug monitoring (Denise A. McKeown, YSC Secretary) and forensic toxicology (Dimitri Gerostamoulos, TIAFT YS Chairman), and provided an excellent forum for open discussions between peers.

Reinier Van Hest (YS member) not only presented the first scientific oral presentation of the congress but set a high standard for the week, which included a further 17 oral and numerous poster presentations from the YS. The YS scientific contribution to the congress was recognised when the awards for the best TDM oral and poster were presented to YS members.

Award References

Therapeutic Drug Monitoring, Volume 29, Number 2, August 2007.

41. F. Saint-Marcoux, J. Debord, G. Hoizey, O. Tribut, M. Canal, G. Sequier, P. Marquet. Statistics of MMF Dose Adjustment on ISBA, a Free Website for Dose Adjustment of Immunosuppressive Drugs.

226. R.R. Press, B.A. Ploeger, J. den Hartigh, R.J.H.M. van der Straaten, J. Van Pelt, M. Danhof, J.W. de Fijter, H.J. Guchelaar. Dose Prediction of Tacrolimus in de novo Kidney Transplant Patients with Population Pharmacokinetic Modelling Including Genetic Polymorphisms.

To discuss and plan the groups future goals the YS held their first IATDMCT Business and Committee meetings. These were well attended and the committee has grown to include a YS website co-ordinator (Tine Dewaele), YS mailing list co-ordinator (Asma Djabri) and six ordinary members (Catherine Wilkinson, Sarah Wille, Susannah Kenyon, Jennifer Button, Reinier Van Hest and Christoph Sauer).

Besides their participation and contributions to the meetings official scientific program and YS events, the YS also enjoyed the social events, meeting each other and “established” scientists. They also spontaneously organized some unofficial YS meetings and trips which were well attended and thoroughly enjoyed by all, indicating the great atmosphere in the YS group.

We would like to thank the YS participants for making this inaugural meeting such a success and look forward to seeing you, and all other YS who could not attend the Nice meeting, in Montreal 2009!

Denise A. McKeown
(YSC Secretary)

Frank T. Peters
(YSC Chairman)

Young Scientists Workshop Report

Welcome

Frank T. Peters, chairman of the Young Scientist Committee (YSC) welcomed all YS attendees to the first YS workshop. Throughout the workshop proceedings Prof. D.W. Holt (President, now Past-President), Prof H.H. Maurer (President-Elect, now President) and Prof. A.A. Vinks (now President-Elect) took time out from their busy schedules to welcome all YS participants on the behalf of the IATDMCT association. Their chosen words showed continuing support for the YS group and recognised the importance of encouraging future generations involvement in the associations activities.

Oral Presentations

Three excellent overview presentations were given to provide YS, especially those new to the field, with an impression of the spectrum, similarities, and differences of various disciplines in the field of therapeutic drug monitoring, clinical toxicology, and forensic toxicology.

“Analytical Strategy for Effective Clinical Toxicology Services.”

F. T. Peters, Homburg, Germany.

An effective clinical toxicology service requires various analytical methods ranging from simple spot test, e.g. for paraquat, to hyphenated mass spectrometric techniques. These have to be integrated into a comprehensive analytical strategy allowing screening, identification and validated quantification of drugs, poisons and/or their metabolites in body fluids. The strategy for effective 24/7 clinical toxicology services in Homburg, Germany, will be presented focussing on examples of screening analysis for new designer drugs in urine using gas chromatography-mass spectrometry after acid hydrolysis, liquid-liquid extraction and acetylation. Examples of quantification of (low dosed) drugs, e.g. modern antipsychotics, using liquid chromatography-mass spectrometry after liquid-liquid or solid-phase extraction will also be presented. The efficiency of mass spectrometry for simultaneous analysis of a broad range of structurally heterogeneous classes of drugs and poisons will be discussed.

Impact of the Introduction of LC-MS/MS Analysis on Therapeutic Drug Monitoring and Endogenous Biomarker Measurements.

D. A. McKeown, London, UK.

Therapeutic drug monitoring (TDM) is used in a variety of clinical settings as a guide to optimising drug therapy. For drugs to qualify for TDM they have to fulfil certain criteria. These include: a narrow therapeutic window, complex and unpredictable pharmacokinetics, the possibility of drug-drug or drug-food interactions and their use in special patient categories such as paediatrics and pregnant women. The use of TDM is well established in immunosuppressive therapy for transplant

recipients, whereas controversy still surrounds the benefits of TDM for antiretroviral therapy in HIV positive patients.

The increasing trend in the use of liquid chromatography-(tandem) mass spectrometry (LC-MS(/MS)) in clinical laboratories is not unexpected when one considers the advantages the technique offers. LC-MS(/MS) lends itself to clinical applications such as the analysis of TDM samples and the measurement of small molecule endogenous biomarkers, because it is highly sensitive and selective, capable of wide linear ranges and allows fast simultaneous multi-analyte analysis with low sample volume requirements. Quick turn-around times and high sample throughput are paramount to the success of busy TDM services. The development of semi-automated online clean up methods such as solid phase extraction (SPE-LC-MS/MS) and turbulent flow chromatography (TFC-LC-MS/MS) has reduced the time taken to process complex sample matrices.

A common misconception is that LC-MS(/MS) offers absolute specificity, whereas, it can suffer interferences that arise from co-eluting compounds, sample matrices and cross talk. The use of deuterated drug analogues as internal standards can reduce the impact of these interferences. However, there is a lack of commercially available stable isotopes for immunosuppressive and antiretroviral drugs. The lack of standardised protocols for the preparation of in-house and commercial calibrators and controls can introduce further errors when analysing patient samples. Whilst initial purchasing costs are expensive, and skilled scientific staff are required to develop methods and operate the equipment, in the long-term it can prove cost effective.

Analytical Challenges in Post-mortem Toxicology.

D. Gerostamoulos. Victoria, Australia.

The need for smarter and more efficient analysis in forensic toxicology is an ever-growing challenge for testing laboratories. The role of the toxicologist is to determine the types of possible substances ingested and then the measurement and confirmation of these substances or products. This is often in the absence of any real information which can direct the nature of testing. Forensic toxicology today encompasses not only traditional coronial cases but increasingly drugs and driving cases, drug facilitated sexual assault cases, and workplace drug testing. All cases can potentially be challenged in court so the need for validated and accredited analytical methods and techniques are essential. This presentation will expand on some of the challenges faced by toxicologists in producing reports as evidence for medico-legal purposes. Case examples will be given to illustrate the complexity of testing, the need to satisfy accreditation requirements and the interpretation of toxicology results; arguably one of the most challenging aspects of being a forensic toxicologist.

Open Forum

As part of the workshop an open forum was held to discuss topics raised during the oral presentations and other items related to attendees research or routine work. This provided an excellent forum for discussion between peers. The following topics were discussed:

- The selection of appropriate internal standards for hyphenated chromatographic systems with mass spectrometric detection. The discussion included selecting suitable internal standards in the absence of deuterated standards (first choice) and structural analogues (second choice). It was also highlighted that problems with matrix effects and interferences in LC/MS(/MS) are not always compensated for when deuterated internal standards are used.
- Methods of sourcing pure reference materials and the difficulties that can be encountered throughout this process e.g. lack of availability, expense. Stability of older reference material stock is often unknown.
- The benefits of measuring metabolites in clinical and forensic toxicology. The lack of availability of numerous metabolites for varying reasons such as the expense of manufacture.
- The investigation into new potential methodology for the biotechnological synthesis of drug metabolites was highlighted and was presented later in the conference week.

Reference

Therapeutic Drug Monitoring, Volume 29, Number 2, August 2007.

23. [Frank T. Peters](#), Andrea E. Schwaninger, Calin A. Dragan, Matthias Bureik, and Hans H. Maurer. New Fission Yeast Strains Expressing Human Cytochrome P 450 Enzymes to be Used for Biotechnological Synthesis of Drug Metabolites.

- The differences in the interpretation of clinical and post-mortem levels.
- Difficulties and importance of matrix matching in post-mortem toxicology. For example, using the appropriate matrix (blood, liver, vitreous humour) to prepare calibrators for appropriate assays.
- Difficulties in interpreting post-mortem toxicology results when considering factors such as lack of fatal and toxic ranges for some drugs and the various sample matrices, pharmacogenomics and post-mortem redistribution.

1st IATDMCT Young Scientists Business Meeting Minutes

Welcome & Opening Remarks from the Chair

- Frank T. Peters the YSC chairman opened the 1st IATDMCT YS Business Meeting.
- Dimitri Gerostamoulos the TIAFT YS chairman summarised the experiences of their group to contribute ideas for the future activities of the group within the association.

YSC Updates

- IATDMCT YS Membership Numbers
The number of YS members increased from 8 in July 2006 to 39 in August 2007, clearly demonstrating that the reduced membership fee proposed by the YSC encouraged YS to join the association.
- IATDMCT YS Attendance at the Biennial Congress, Nice 2007
A further achievement of the YSC is the negotiated reduced Congress fee for YS, indicated by 31 conference delegates being registered as “Young Scientists”.
- YSC were pleased to report that the YS were contributing numerous oral and poster presentations to the Congress programme.
- Thank you to Sarah Wille who volunteered to be the YS roving reporter for 'The Daily Compass' newsletter published during the Congress.

YS Biannual Scientific Issues Series for “The IATDMCT Compass”

- Thank you for the following articles contributed to the compass:
“Matrix effects in LC-MS” (Frank T. Peters & Denise A. McKeown).
“Solid-phase extraction in clinical toxicology” (Sarah Wille).
“Piperazines – the new emerging recreational drugs” (Jennifer Button & Susannah Kenyon).
- The following article is planned for the 2007 4th quarter issue:
“New Trends in Herbal Drugs of Abuse” (Jochen Beyer).
- All YS members were encouraged to submit suggestions for topics, for the two articles that will be published in 2008 Issues 2 and 4, to Frank T. Peters and Denise A. McKeown.

Committee Posts

- The following committee posts were proposed and accepted; coordinator for the YS corner of the website, coordinator for the YS mailing list and ordinary members to assist in the planning and organisation of future YS activities.
- All YS members were welcomed to attend the YSC lunch meeting (Wednesday 12th September) were volunteers for these posts would be considered and the roles filled.

Discussion and Ideas for what YS Members want to Gain from this Group

- Positive feedback was given regarding the YS informal lunch at the start of the conference, a good time was had by all. Good format for future Congresses.
- YS would like to see a further reduction in Congress fees for YS under 31 and students, approximately half that of members. YSC explained that the fee is not set by the association but by the conference organisers, they will investigate this possibility.
- YS would like the YS workshop to be free in addition to the one free workshop that was included in the Congress registration. YSC explained that was the intention, however, due to matters outside their control it was not possible for this Congress but plan to ensure the workshop is free for the 2009 Congress. YSC also added that the free workshop included in the congress registration fee was again set by the conference organisers not the association.
- YSC plan to have dedicated YS prizes for orals and posters at the 2009 Congress.
- YSC proposed that YS events are open to members up to 40 years; however, the YS discount category will remain as it is, accepted by all.

Themes for Future Workshops

- YS agreed that the general overview oral presentation format and the open forum discussion was successful and felt that this was a good formula for future meetings.
- All agreed that the YS business meeting should be held separately, outside the workshop time slot.

Meeting Closed

Young Scientists Committee Meeting Lunch Minutes

- Frank T. Peters the YSC chairman opened the 1st IATDMCT YS Committee Meeting.
- The YS Committee posts were discussed and the roles appointed.
- Tine Dewaele, Ghent University, Belgium, filled the position of coordinator for the YS corner of the IATDMCT website. This is a critical role in increasing the presence of the YS group within the association and to potential new members who visit the site. The website will allow YS to post articles, photos, planned events etc.
- Asma Djabri, University of Bath, UK, filled the position of coordinator for the YS mailing list. Keeping an up-to-date mailing is critical in ensuring that all YS members are kept informed of the groups activities and will allow easier communication between members.
- Six Ordinary members were appointed. Their roles are crucial in helping with committee work especially during the future Congresses. The following YS filled these positions; Catherine Wilkinson (University of Western Australia, Australia), Reinier Van Hest (Erasmus MC, The Netherlands), Christoph Sauer (Saarland University, Germany), Sarah Wille (Ghent University, Belgium), Jenny Button (St George's – University of London) and Susannah Kenyon (St George's – University of London).
- It was proposed to try and organise the YS workshop so that it does not parallel the more popular workshops. This would allow more YS to attend without missing critical learning opportunities that can be gained from other workshops.
- YS events will be open to members up to 40yrs, it is important to have more experienced members within the committee who have the experience to drive forward the groups ideas, organise events and to communicate and negotiate the YS needs with the association.
- YS suggested funding a developing country YS member to attend the Congress. The YSC reported that the IATDMCT already hold a developing countries fund, they also provide further discounted membership and Congress fees.

- YS members with special dietary requirements raised concerns that these were not always met during the Congress, although they paid their Congress fee. YSC reported that the catering is not necessarily part of the fee, lunches are not always provided, it depends on the level of sponsorship. However, the YSC will put forward these concerns to the organising committee for the 2009 Congress.
- YSC thanked all the YS for their participation.

Meeting Closed

IATDMCT Annual General Meeting

Frank T. Peters (YSC Chairman) provided feedback of the YS activities and progress at the AGM.

IATDMCT Council Meeting

Frank T. Peters (YSC Chairman) and Denise A. McKeown (YSC Secretary) were invited to the meeting of the Council of the IATDMCT to put forward the YS views and ideas. The following points were proposed to the Council:

- YS events should be open to members up to forty years, however, the discount category to remain as it is currently.
- Future YS workshops to be free to YS members and that sponsorship would be required for this.
- For future Congresses would it be possible to avoid the YS workshop being scheduled at the same time as the more popular workshops so that YS don't miss out on either opportunity.
- How to coordinate contacting all YS members under 40 years, especially those not in the YS discount category, for example those under 40 and developing country members?
- To have dedicated YS awards for orals and posters at future Congresses.

During the meeting the YSC were introduced to the organisers of the 2009 Congress in Montreal, who are keen to communicate with YS group during the organisation of the 2009 Congress.