2018 IATDMCT Congress
Top science down under
16–19 September 2018 Brisbane, Australia

Sunday pre-congress symposium

Drugs of use and misuse, Pharmacogenetics and Pharmaco-Justice

This symposium will review the legal definition of therapeutics-induced drug of use and misuse-induced adverse events (ADRs), and how it is applied by immunogenetic and toxicogenetic to in vitro diagnostic tests. Hypersensitivity reactions to drugs of use and their possible interactions with drugs of misuse lead to liver failure, akathisia, Steven Johnson syndrome. Therapeutic interventions should be monitored by clinicians and laboratory as well. Genetic variations should be studied in the laboratory and tailored in practice by the clinicians. The substance harm has lately been aggravated by a drug market that also sells products whose composition is not disclosed to the users; it is becoming more and more common that such products comprise not of single drugs but of multiple drugs whose purity and/or actual combination can lead to severe side effects. This presentation highlights the crucial role the clinical laboratories can have in collaborative harm reduction strategies. Genetic variations in metabolism affect how different people react to anti-depressants, and now medical examiners Finally, the proposed Laboratory. Clinical studies of psychiatric patients treated for their illness with emphasis on recommendations for use of pshycho-pharmacogenetics tests will be discussed.

Audience profile: laboratory directors, technologists, managers, physicians, pharmacists, neurologists.

Congress symposia

Symposium 1: Therapeutic drug monitoring of mycophenolic acid products: Evidence and knowledge gaps, laboratory and clinical experience

The use of therapeutic drug monitoring (TDM) to optimise MPA product dosing remains controversial and variably applied in clinical practice. This is in part due to conflict in the literature, and in part due to the cost and practical implications of AUC estimation, the exposure metric with the best (RCT) supportive evidence.
Nevertheless, given the consequences of over- and underexposure to mycophenolic acid products, the use of TDM has continued at many centres and more broadly there is a re-emergence in interest.

Practice varies, however, on multiple levels. These include:

- The assay used: EMIT versus HPLC
- Measurement of MPA-glucuronide or unbound MPA concentration, in addition to total MPA
- The exposure metric: trough MPA concentration or AUC estimation
- The technique for AUC estimation: trapezoidal AUC, multi-linear regression or Bayesian forecasting
- The frequency of testing, particularly where AUC estimation is used
- The optimal target concentration in varying populations

Through discussion of (a) the strengths and limitations of the available evidence, (b) knowledge gaps, (c) harmonisation of techniques for measurement and interpretation of concentrations, and (d) sharing of clinical experience, we hope to provide a blueprint for utilisation of TDM in clinical practice, and for future research.

Audience profile: clinicians, pharmacologists, pharmacists and laboratory scientists involved with the use or measurement of mycophenolic acid (MPA) products.

2018 IATDMCT Congress
Top science down under
16–19 September 2018 Brisbane, Australia

Symposium 2: Immunogenetics and Drugs of Use and Misuse

This symposium will the role of immunogenetic in monitoring safety and efficacy of therapeutics as well as the role of gene world association in patients suffering from alcohol and drugs of misuse disorders. Identification of drugs or biologics with potential to cause serious, life-threatening drug-induced injury requires causality assessment and comprehensive testing for alternative etiologies in each suspected case. Since idiosyncratic drug-induced-injury is rare, prediction of the risk of serious drug-induced-injury post-marketing relies on identification of cases of interest meeting criteria during phase II-III clinical trials. Subjects with pre-existing, chronic liver diseases (CLDs), or chronic renal impairment, with or without cirrhosis, are challenging because current FDA guidance is based largely on criteria for studies that exclude subjects with abnormal liver or renal tests. CLDs do not increase overall susceptibility for drug-induced liver injury (DILI), but multiple exceptions suggest that additional examples will be identified in future clinical trials. DILI in subjects with CLD is worrisome because subjects with reduced hepatic functional reserve are less likely to recover and more likely to die. The probability of subjects with CLDs enrolling in clinical trials is increasing, especially in therapeutic trials targeting components of the metabolic syndrome, antimicrobials, complications of cirrhosis and hepatocellular carcinoma.

Therapeutic interventions should be monitored by clinician and laboratory as well. Genetic variations should be studied in the laboratory and tailored in practice by the clinicians. Monoclonal antibodies are used against inflammatory diseases. Definition of laboratory test and how it has been interpreted by clinician will be review. The reduce efficacy of the antibodies in time and the possible adverse reactions that they can produce due to immunogenecity will be explained. Moreover, therapeutics and Drug monitoring of therapeutics used in cancer are link to immuno-pharmaco-genetics.

Audience profile: Laboratory scientists, technologists, managers, physicians, pharmacists, neurologists.

Symposium 3: Should we routinely measure unbound drug concentration?

Total drug concentrations are routinely measured in therapeutic drug monitoring. Unbound drug is in equilibrium with the site of action at steady state. In healthy people there is close correlation between total and unbound drug concentrations. However, the times of critical decision making are when physiology is not normal. In altered physiological states, such as critical illness, the bound concentration typically decreases and total concentration can be misleading. Most published data, and reference ranges, refer to total drug concentrations in healthy populations. Unbound drug concentration can be measured directly after equilibrium dialysis or ultrafiltration, or can be calculated. This potentially increases result uncertainty and analytical cost. This symposium will discuss the use of unbound and total drug concentrations in clinical care from clinical, analytical and pharmcometric perspectives.

Audience profile: clinicians and laboratory scientists involved in the interpretation of drug concentrations.

2018 IATDMCT Congress
Top science down under
16–19 September 2018 Brisbane, Australia

Symposium 4: Pre-emptive Pharmacogenetic testing

There is a growing interest in identifying the most effective way of integrating pharmacogenetic testing into a variety of healthcare environments. One approach that has been proposed as being both cost effective and enabling rapid and efficient utilization of PGt test results, is to test candidate patients for a panel of PGt genes in a pre-emptive mode that may or may not include a trigger-event.

This session will introduce the rationale and driving forces, (e.g. incidence of polypharmacy) for this concept and provide an overview of the background literature as an introduction. We will then have thought leaders to present their experience with this approach. Study design and results from a large European multi-site study will be presented as well as the experience of a major healthcare center which has adopted this approach into routine care of patients.

Audience profile: laboratory directors, clinical pharmacologists, clinical pharmacists and clinical biochemists who are evaluating best practices for effective and cost effects implementation of pharmacogenetics services.

Symposium 5: TDM for antiviral agents

The use of therapeutic drug monitoring to optimise antiviral drug treatment remains controversial and variably applied in clinical practice. For several drugs, including valganciclovir, ribavirine, and antiHIV-drugs there is a lot of discussion on whether or not to monitor drug concentrations.

In this workshop the available evidence will be reviewed, clinical experience will be shared, and opportunities for future research will be identified. By bringing together IATDMCT members with an interest in this field mutual projects can be initiated.

Audience profile: clinicians, pharmacologists, pharmacists and laboratory scientists involved with the use of antiviral agents.

Symposium 6: Education in TDM and CT

Therapeutic drug monitoring and clinical toxicology has a rather short history. Educational matters have hitherto not been a subject at the IATDMCT conferences. The importance of educating a new generation of TDM&CT professionals is of ever growing clinical importance. TDM&CT is very differently organized at different sites and in different countries.

The aim of this symposium is to inspire and promote educational activities in an international perspective by highlighting some good examples of curricula and teaching modalities in graduate, postgraduate and continuing workplace education.

Audience profile: participants involved in or subjected to different educational activities in the field of therapeutic drug monitoring and clinical toxicology, regardless of profession

---

2018 IATDMCT Congress
Top science down under
16–19 September 2018 Brisbane, Australia

Symposium 7: Microsampling and dried blood spot analysis

This symposium will provide an overview on available microsampling strategies. Besides dried blood spot and volumetric absorptive microsampling, other techniques will be discussed. The pros and cons of the different techniques will be discussed. In addition to the overview an in-depth analysis of dried blood spot implementation in daily practice will be presented. Analytical challenges as well as practical and clinical issues will be discussed. Moreover the application of microsampling in a vulnerable population, ie critically ill children, will be presented. Practical and ethical issues will be addressed.

Audience profile: laboratory and clinically oriented TDM and PK minded professionals.

Symposium 8: Medicalization and legalization of Cannabis: Short and long-term consequences

This symposium outlines the specific issues affecting medical practice with cannabinoids and the role that TDM can play in facilitating knowledge of dose and effect.

Audience profile: clinicians, laboratory analytics, pharmacists, preclinical scientists including plant scientists.

Symposium 9: Dosing Decision support tools in special populations: Paediatrics

More information coming soon

Symposium 10: *Staphylococcus aureus* blood stream infection mortality is still 30%: Could TDM make a difference?

Staphylococcus aureus remains the most common pathogen in the majority of studies of both community- and hospital acquired blood stream infection. Despite the availability of antibiotics with excellent *in vitro* activity against *S. aureus* attributable mortality reaches 30% in many published studies. Until recently there was little interest in therapeutic drug monitoring of anti-staphylococcal drugs other than vancomycin. There is now a slowly growing body of literature concerning alternative treatment agents such as the anti-staphylococcal beta-lactam agents, clindamycin, rifampicin, fusidic acid, linezolid, telizolid, tecoplanin, dalbavancin and daptomycin. The role of therapeutic drug monitoring to optimise therapy with each of these agents will be discussed in this symposium with the aim of making dosing recommendations to improve patient outcomes.

Audience profile: academics, clinicians, and industry scientists involved in therapeutic drug monitoring.

Symposium 11: Alternative matrix for the determination of human exposure to environmental pollutants

Information about human exposures to environmental pollutants is a crucial component of health-risk assessment for the protection of public health. Human exposure to environmental pollutants is commonly assessed using standards matrices such as urine or blood. Alternatively, other matrices can be used to improve exposure assessment. Colostrum and mature breast milk can provide accurate estimates of infant's exposure to environmental

contaminants in the neonatal period. Adipose tissue can also be used to assess accumulation of environmental pollutants at the target site of action.

The objective of this symposium is to demonstrate the usefulness of these alternative matrices for human exposure assessment to environmental pollutants. Analytical methodologies for analyzing those matrices will be discussed. An example of the analysis of pesticides in food matrices will be also given during this symposium.

Audience profile: toxicologists and analysts.

Symposium 12: Debate – Genotyping of cancer tissue to advise choice of chemotherapy is pharmacologically unsafe

Millions of dollars, in many jurisdictions, has been spent on pathology testing for biopsies of tumours to help predict response to therapies. Although this sounds simple and exciting, this neglects the basic tenets of basic and clinical pharmacology. It also presupposes that the biopsy is representative of the tumour, that the tumour is homogenous in its mutational state, and that the original tumour sequencing is consistent with the profile at relapse. It is understandable that Pharmaceutical companies use this strategy to enable access to a small population for a very expensive drug, for a population that can be expanded subsequently, however there has been concern that people who may benefit have missed out and that people who have a mutation haven't responded. Advocates however argue that huge increases in understanding of molecular biology has been a reasonable endpoint and that improved outcomes have been seen in some patients. Patient advocates say can offer hope to patients at the end of conventional therapy. But has the investment efficient? Has the focus on gene therapy in cancer harmed or helped patients. Two teams of pathologists, cell biologists and clinical pharmacologists argue the for and against in a tense session chaired by one of Australians leading clinical oncologists.

Audience profile - basic and clinical pharmacologists and toxicologists, cell biologists/molecular biologists, anatomical pathologists, clinical oncologists.

Symposium 13: The translational science of antidoping – investigating pure performance

This symposium will highlight major developments in the science and translational application of antidoping. Australia has been an innovator and leader in the area of antidoping over recent decades. This symposium will showcase that expertise.

Analytical innovations in antidoping – staying ahead of the cheats - The forefront of antidoping science is moving quickly – and must do so to meet the global threats of antidoping and corruption in sport

Translational antidoping – track to the clinic - Insights from the WADA Health Medical research committee where antidoping is translated into policy and practice– especially with a focus on future developments and innovations. The implications for clinical practice and the health impacts on athletes will also be covered.

Innovations and logistics – delivering a modern testing program for the games - A feature of the symposium will include critical insights on the challenges of delivering a major testing mission of the Commonwealth Games (Gold Coast, April 2018)

Audience profile: analytical scientists, hospital scientists, clinical pharmacologists, sports physicians, pharmacists, national antidoping bodies.

2018 IATDMCT Congress
Top science down under
16–19 September 2018 Brisbane, Australia

Symposium 14: Emerging TDM technologies and obstacles to widespread use

Technologies are emerging that allow clinicians to better individualize patient dosing regimens. Monte Carlo simulation based tools allow clinicians to select initial dosing regimens optimized based on patient demographic information. After therapy starts, plasma concentrations can be utilized in a Bayesian-based software program (also known as a closed loop control system) to further individualize doses. Moreover, some tools can also utilize biomarker data, which allows for further dose adjustments based on various markers of drug response. The first part of this symposium will focus on introducing the audience to these new technologies.

Many of these tools are now available at the patient bedside and are becoming easier to use through their user-friendly interfaces and integration into electric health record systems. However, despite these advances, pharmacometric-based dose selection and therapeutic drug monitoring have not been widely adopted in clinical practice. The second part of this symposium will focus on identifying the barriers and gaps hindering the widespread adoption of these tools in clinical practice. Clinical thought leaders from various countries will share their experiences and thoughts on the issues and potential paths forward, culminating in an open forum that will chart the path towards increased utilization.

Audience profile: academicians, clinicians, and industry scientists involved in therapeutic drug monitoring.

Symposium 15: Screening for novel psychoactive drugs in clinical and post mortem toxicology

In this symposium we will present state-of-the art analytical techniques that can detect novel designer drugs as well as potential overdoses of conventional drugs in patients. These techniques do shorten turn-around times and make toxicology screening in clinical situation feasible. Further, we will address what skills are needed to obtain relevant results with these techniques and how to interpret the data to give the emergency physicians the relevant information that will help to diagnose an intoxication and to select the best treatment of intoxicated patients. How to design an extensive screening on (novel) drugs in post mortem blood and urine? How to report these results to coroners? How to speed up the turn-around time of toxicological investigations and still obtain more relevant information?

Learning objectives:

1) Novel Psychoactive Drugs: Impact on Clinical and Forensic Toxicology.
2) Drugs screening in clinical toxicology: real life complex cases.
3) LC-MS techniques potentials and limitations in the clinic.
4) What quality control do we need for clinical and post mortem toxicology screening?
5) Do we still need immunoassays in toxicology screening?
6) Drugs screening in post mortem toxicology: surprising cases.
7) Clinical impact of drug screening for patient management.

Audience profile: clinical toxicologist, emergency room physicians, pharmacologists, laboratory specialists, pathologists, clinical chemists, laboratory technicians.

2018 IATDMCT Congress
Top science down under
16–19 September 2018 Brisbane, Australia

Symposium 16: IATDMCT Young Scientist Symposium

The symposium will offer YS the opportunity to hear and learn from experienced scientist about latest developments and emerging topics within the field of TDM and CT. The symposium should initiate the scientific exchange amongst YS and generate new ideas.

Audience profile: Mainly young scientists, but also open to an 'older' audience.

Monday morning roundtable sessions

PK/PD of commonly used antibiotics: Do plasma concentrations reflect tissue concentrations?

Facilitated by the Anti-Infective Drugs Committee
More information coming soon

Implementation of TDM in vulnerable patient groups with refractory epilepsy with case examples

Aim: To share experience and elucidate the impact of TDM in vulnerable patient groups with refractory epilepsy at a referral center for individualized treatment. We aim at discussing principles and clinical cases of pharmacokinetic variability in relation to efficacy and tolerability of the newest antiepileptic drugs in children and adults how women using valproate may be monitored for improved safety of mother and fetus, and how TDM may be used for optimal treatment outcome.

An approach of pharmacokinetics and clinical evaluation of new antiepileptic drugs will be discussed with several examples, and the impact on clinical care will be addressed. The proposed symposium will focus on clinical implications and handling. In Norway we have long-term experience in using TDM as part of a comprehensive care approach to individualize the therapy, and we have a collaboration between the national epilepsy centers in Norway and Denmark regarding development of new analytical methods and use of TDM. Various vulnerable patient groups will thus be discussed in this symposium, and the usefulness of TDM will be highlighted.

Audience profile: researchers, clinicians and pharmacologists working within the field of epilepsy.

Tuesday morning roundtable sessions

Controversy around vancomycin target to achieve optimal therapeutic effect: Trough only or both peak and trough levels, AUC/MIC ratio versus Cmax/MIC ratio: Where is the evidence based practice?

Facilitated by Hundie Tesfaye, Motol University Hospital; Charles University, Prague, Czech Republic

Vancomycin is antibacterial used as a drug of choice predominantly for MRSA. Mainly due to potential toxicity, it is common practice to monitor its serum levels, provided that is meaningful only if target concentration to be achieved in an individual case is certain. Since vancomycin kills bacteria in a time-dependent manner, it is important to ensure that the trough concentration remains above the MIC for the organism being treated. Previously, target trough level was aimed based on the theoretical aspect that, more than 90 % of the sensitive agents have MIC 1-2 mg/L or less. Nowadays, there are emerging suggestions advising trough levels 15-20 mg/L,

despite lacking evidence of superiority. The fact that many studies have methodological shortcomings on safety and efficacy testing challenges the quality of the information published. Some review papers involving many aspects of Vancomycin PK/PD are published recently; Nevertheless, there is no convincing guidelines especially on what is relevant as dynamic predictor and whether loading dose is so important for final outcomes. The dosing schedule for special populations (paediatric, geriatric, and critically ill patients) should be discussed during the symposium /workshop reflecting the real clinical problems in context with patient factors.

Audience profile: clinicians, microbiologists, clinical pharmacologists, pharmacists, biochemists, analysts.

Identification and handing of pharmacokinetic interactions of antiepileptic- and psychoactive drugs with case examples

Chair: Assoc Prof Cecilie Johannessen Landmark, Oslo Metropolitan University and The National Center for Epilepsy, Oslo University Hospital, Norway
Co-chairs: Dr Arton Baftiu, Oslo Metropolitan University; The National Center for Epilepsy, Oslo University Hospital, Norway and Dr Tore Haslemo, Center for Psychopharmacology, Diakonhjemmet Trust Hospital, Oslo, Norway

Aim: To increase awareness of polypharmacy and interactions with antiepileptic drugs (AEDs) and other psychoactive drugs (antidepressants and antipsychotic drugs), and to give practical advice in handling these situation in clinical practice.
Polypharmacy with antiepileptic drugs is common, and the possible pharmacokinetic interactions are numerous. It is well known that about one third of patients with epilepsy also suffer from psychiatric comorbid disorders. Polypharmacy with up to 8-9 CNS-active drugs are seen. The consequences of inappropriate handling are seizure worsening or toxicity. Many patients live with a heavy adverse effect burden, leading to poor adherence and a decreased quality of life. The proposed symposium will focus on clinical implications and handling with cases related to the specific topics.
The process from identification to handling of commonly occurring interactions with clinical cases will be highlighted in this symposium.

Audience profile: researchers, clinicians and pharmacologists working within the field of epilepsy and psychiatry.

Hematocrit and dried blood microsampling: Still an issue?

Facilitated by Assoc Prof Jan-Willem Alffenaar, University Medical Center Groningen, The Netherlands
More information coming soon

Wednesday morning roundtable sessions

Renal replacement therapy modalities and the PK of antimicrobial agents

Facilitated by the **Anti-Infective Drugs Committee**
More information coming soon

How do we do better to deal with dosing errors in children?

Facilitated by Assoc Prof Catherine Sherwin, University of Utah School of Medicine, USA and Dr Hesham Al-Sallami, University of Otago, New Zealand

Errors associated with medications are common in children with up to 27% of all paediatric prescriptions associated with a medicine error and 0.24% resulting in significant morbidity and mortality. Children are at high risk for these errors partly due to in accurate scaling of drug dose. To reduce this preventable harm, we need to understand the various mechanisms of these errors and also to develop, evaluate, and implement interventions to reduce them and mitigate their impact.

In this symposium, we will cover the mechanics of drug dose-response in children and dose scaling from adults. The pharmaco-epidemiology of paediatric medication errors and current tools and interventions used to reduce their frequency and impact will be discussed.

Audience profile: Pharmacists, physicians, clinical pharmacologists, and pharmaco-epidemiologists interested in therapeutics, clinical pharmacology, drug dosing, and medication errors.

2018 IATDMCT Congress
Top science down under
16–19 September 2018 Brisbane, Australia

Wednesday post congress workshops

Bridging the Gap Between Bayesian-based TDM and Traditional TDM

Facilitated by Elizabeth Lakota, Institute for Clinical Pharmacodynamics, USA

Bayesian-based therapeutic drug monitoring (TDM) enables dosing regimens to be individualized for patients using sparsely collected pharmacokinetic samples through pharmacometric analyses. Moreover, this method is preferable to traditional TDM given that it allows for more personalized dosing adjustments, which can lead to improved efficacy and decreased toxicity. Additionally, these benefits can be obtained through the use of fewer pharmacokinetic samples than ordinarily required for traditional TDM, thus saving both time and money. This workshop will be comprised of three parts:

1. Participants will be introduced to the elements needed to perform adaptive feedback control (AFC), including TDM. These elements include a therapeutic target window based on dynamics of efficacy and toxicity, availability of suitable assay, turnaround time of assay, an optimal sparse sampling strategy, a validated Bayesian-based software and a team of adequately trained clinicians who can implement AFC at the bedside.

2. A deep dive into Bayesian-based TDM through case studies. The examples presented will highlight the development, implementation, and results of Bayesian-based TDM.

3. A focus on how to move the field of TDM forward. Barriers to widespread use of Bayesian-based TDM will be presented, which include issues surrounding the integration of Bayesian software into electronic medical records and the urgent need for the training of clinical staff in basic pharmacometrics. Lastly, future areas of expansion for Bayesian-based TDM, including the use of pharmacodynamic and toxicodyanmic measures, will be discussed.

Medicalization and legalization of Cannabis: Hot topics

This symposium will outline the specific issues affecting medical practice with cannabinoids and the role that TDM can play in facilitating knowledge of dose and effect.

Audience profile: clinical, toxicology, pathology, plant scientist.
