INVITED SPEAKERS

Professor James Dear

is a Clinical Toxicologist performing translational research, taking clinical problems across the scientific-clinical interface, identifying solutions and applying new ideas in patients. As an example of delivering research that has a meaningful impact on human health, Professor Dear was part of the team that developed a shorter 12-hour treatment regimen with the antidote acetylcysteine ("SNAP") for acetaminophen overdose, and in a randomised clinical trial found it to result in fewer adverse drug reactions (ADRs) and be as effective at preventing liver injury as the standard 21-hour treatment. TOXBASE, the UK's primary authority on poisoning cases, was updated to recommend SNAP in April 2020, meaning that all approximately 50,000 annual hospital admissions for acetaminophen overdose can now be treated according to the SNAP regimen. This translates to savings of up to $10,000,000 every year.

1. Optimising Paracetamol Overdose Management: Global Perspectives and Innovations

This symposium on paracetamol (acetaminophen) overdose management aims to explore the multifaceted aspects of treating paracetamol poisoning worldwide. With a global expert panel, the symposium will delve into the assessment and management of paracetamol poisoning, highlighting significant regional variations in approaches.

The symposium will begin by examining specific regional practices in paracetamol overdose management, focusing on Sri Lanka as a case study to illustrate key differences in protocols and clinical outcomes across diverse healthcare settings. This comparative analysis will provide valuable insights into the impact of regional healthcare infrastructures on patient care.

This symposium will also discuss which patients may require more antidote (acetylcysteine). Examining the scenarios and evidence supporting escalated administration of acetylcysteine and the different acetylcysteine regimens used.

Lastly advancements in biomarkers and novel antidotes will also be a focal point. With a discussion of potential emerging liver biomarkers and their utility in paracetamol poisoning. Followed by a review of the research for novel antidotes.

The symposium will culminate in a panel and audience discussion featuring compelling case studies of paracetamol overdose from diverse geographical contexts. Participants will analyse and debate the varying approaches to management, and how infrastructural differences, and healthcare system disparities, that influence clinical decision-making worldwide. This symposium promises to provide a thorough exploration of global perspectives and innovations in paracetamol overdose management.

2. My research journey – paracetamol poisoning

Paracetamol overdose is a common medical emergency. Across the UK, »100,000 people attend hospital following a paracetamol overdose every year (one every 5 minutes, same as myocardial infarction) and around half need admission for treatment with the antidote acetylcysteine (n-acetylcysteine – NAC). Around 10% will get biochemical evidence of liver injury and ~2-3 people die from paracetamol-induced liver failure every week. It is more common in Scotland than any other UK region, or indeed globally.

There is a lack of robust evidence to guide treatment decisions. The Cochrane Library published a systematic review of interventions for paracetamol overdose in 2018. The conclusion starts with 'These results highlight the paucity of randomised clinical trials comparing different interventions for paracetamol overdose and their routes of administration and the low or very low level quality of the evidence that is available.' This situation has resulted in differences in treatment

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protocols across countries that are not evidence-based and do not have adequate safety assessments. High dose NAC and repurposed, expensive, drugs are being recommended for off-label use, yet no randomised controlled trials (RCTs) have been performed.

To address the lack of a robust evidence base we have developed biomarkers for drug toxicity. Biomarkers allow early exclusion of liver injury and facilitate prompt identification of injury that will progress despite current treatment. Improved identification of drug-induced liver injury is also of great importance to the pharmaceutical industry in the UK and worldwide. To drive forward our research we have partnered with pharma to translate academic research into commercial benefit and safer medicines for the public.

In parallel with this biomarker program, we have developed a new shorter and safer treatment protocol for paracetamol overdose that is now being used across the UK. We are also developing novel treatments for those patients at high risk of liver failure, a group without effective treatments. This includes leading multi-centre trials of new first in class therapeutics and Advanced Therapies such as cell therapy to repair the injured liver.