Irish Association of Pharmacologists

21st Annual Meeting

Friday, 05th November 2021 11:00am– 4:00PM

Hosted by

The University of Limerick School of Medicine

Welcome to the Irish Association of Pharmacologists 2021

Dear Colleagues,

It is our great pleasure to welcome you to the Irish Association of Pharmacologists meeting for 2021. Greetings to all existing IAP members and also those of you who are joining us for the first time.

After a one-year hiatus due to the COVID-19 pandemic, we are delighted to have you attending in person at the Clinical Education and Research Centre and also to welcome those joining us virtually.

This year there are a variety of excellent speakers who will deliver stimulating input on a variety of aspects of pharmacology, ensuring there is something of interest to all participants.

The AGM is scheduled for early afternoon and all IAP members are encouraged to attend.

With every good wish for an enjoyable meeting

Anne Harnett **Mary B. O'Connell**

Irish Association of Pharmacologists 21st Annual Meeting

Friday, 05th November 2021 11:00am– 4:00PM at

The Clinical Education and Research Centre (CERC) located on the University Hospital Limerick campus

Event	Title	Time
Arrival	**Arrival & Coffee**	**From 10.30**
Welcome	**Professor David Williams – IAP President**	**11.00-11.10**
Keynote 1	**Professor Dermot Cox** **Royal College of Surgeons in Ireland** The Pharmacology of Covid-19	**11.10-11.40**
Short Oral presentations:	**Rasha Alshaikh** **University College Cork** Sphingosine 1-phosphate, a potential target in neovascular retinal disease.	**11.40-11.50**
	Ciara Mc Carthy **University College Cork** Evaluation of cytotoxic activity and chemosensitisation of acute and chronic ethanolamine treatment on oesophageal squamous cell carcinoma	**11.50 – 12.00**
	Rosie Mc Garvey **Queen's University Belfast** Investigation of the NLRP3 Inflammasome in Urothelial Cancer	**12.00 - 12.10**
Lunch	**Lunch and viewing of posters**	**12.10 – 12.55**

Keynote 2	**Dr. Cormac Kennedy** **St James' Hospital & Trinity College Dublin** Clinical Pharmacologists: Jacks of All Trades....	**13.00-14.00**
AGM	**AGM of IAP** coffee	**Approx 14.00** **Tutorial room 1 &2**
Presentations	**Dr. Ahmed Gabr St. James' Hospital and Trinity College Dublin** Implication of an Intracerebral Cerebral Haemorrhage Care Bundle	**14.30-14.50**
	Dr. Hongying Chen University Hospital Limerick Recent Advances in Dementia Management - Aging, Alzheimer's, and Aducanumab	**14.50-15.10**
Short Oral presentations:	**Focus on paracetamol**	**15.10 - 15.40**
	Michelle Byrne **University Hospital Limerick** Paracetamol: From simple analgesic to hepatotoxin.	**15.10-15.20**
	Dr. Jennifer Kearns **Midlands Regional Hospital, Tullamore** Appropriate use of a High Risk Medication: Audit of IV Paracetamol use in a Level Four Hospital	**15.20-15.30**
	Dr. Ruadhan O' Laoi, **St. James' Hospital** A retrospective analysis of paracetamol poisonings and n-acetylcysteine administration in a major teaching hospital.	**15.30-15.40**
Prize Giving and Close	**Professor Deirdre McGrath** Head of School School of Medicine, University of Limerick	**15.40-16.00**

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Speaker Profiles

Welcome Address; Professor David Williams, Royal College of Surgeons in Ireland

Professor David Williams qualified in Trinity College Dublin in 1994. He was awarded a PhD in 2002 for his work on pharmacoepidemiology. Following completion of Higher Medical Training at St James Hospital, Dublin he was appointed consultant Clinical Pharmacologist and Stroke Physician in Aberdeen in 2002. He served as Clinical Vice-President of the British Pharmacological Society from 2007 to 2010. He is currently the managing editor of the European journal of Clinical Pharmacology. In 2009, he was appointed Associate Professor in Geriatric Medicine at the Royal College of Surgeons in Ireland / Beaumont Hospital, where he has helped develop the Acute Stroke Service and undergraduate teaching curriculum in Geriatric Medicine. He is currently the National Speciality Director of training for Clinical Pharmacology and Therapeutics. He is Co-Director of the Irish Clinical Academic Training(ICAT)Programme and Irish Stroke Clinical Trials Network (SCTNI).His research interests include Stroke Medicine, Hypertension, Patient Safety, Prescribing and Medication Errors.He was appointed Professor of Stroke Medicine in 2018.He was elected president of the Irish Association of Pharmacologists in 2019.

Keynote Address: Professor Dermot Cox, Royal College of Surgeons in Ireland

Prof Dermot Cox graduated with a BSc in Pharmacology (University College Dublin, 1983) and a PhD in Immunology (Dublin City University, 1989). He then led a GPIIb/IIIa antagonist drug project in Fujisawa Pharmaceutical Company, Osaka, Japan for 6-years. Following that, he worked for one year in University of Sheffield where he started his work on platelet-bacteria interactions. He subsequently joined Royal College of Surgeons in Ireland where he is currently the pharmacology lead. He also acted as consultant to a number of pharmaceutical companies for both their pre-clinical and clinical programmes. He has taught modules on drug discovery & development on a Masters in Pharmaceutical Medicine programme. He is an academic editor for PLOS One and sits on the advisory board of Journal of Thrombosis and Haemostasis. He was meeting president for International Society on Thrombosis and Haemostasis SSC meeting in 2018.

Keynote Address: Dr Cormac Kennedy, St James' Hospital & Trinity College Dublin.

Cormac Kennedy is currently a Consultant Clinical Pharmacologist and Physician at St James Hospital as well as a Clinical Senior Lecturer at Trinity College Dublin. His experience gives him a perspective of the journey of medicines from the bench to the bedside including the pharmaceutical, regulatory, economic, policy and clinical contexts.

Cormac is a graduate of UCD Medical School and the School of Pharmacy Trinity College. He completed a PhD at the Royal College of Surgeons in Ireland, the product of which was subsequently patented.

He received a HSE-NDTP Management and Leadership Scholarship to undertake a Masters in Health Economics, Outcomes and Management at the London School of Economics and was awarded a Distinction. He is undertaking a Masters in Clinical Trials at Oxford University.

His clinical interests include the specialist treatment of hypertension and lipid disorders and he has presented internationally and published in these areas. His other research interests are across a spectrum of areas related to medicines including pharmacoepidemiology, pharmacoeconomics and appropriate drug usage.

Dr Ahmed Gabr, St. James' Hospital and Trinity College Dublin

Dr Ahmed Gabr is a Specialist Registrar in Therapeutics & Clinical Pharmacology. Throughout his training he has developed a special interest in stroke medicine and service development. He has completed the European Master in Stroke Medicine with distinction (Danube University, Austria in conjunction with the European Stroke Organisation).

He has represented ULHG nationally at the National Thrombectomy Quality Improvement Program and led out on the development of an Intracerebral Haemorrhage Bundle of Care at UHL. He is a member of the Stroke Simulation Group ULHG and has delivered inter- disciplinary stroke simulation training. He has a keen interest in research, participating in clinical trials including CONVINCE, Alpha1- Antitrypsin in COVID and SOLAR-Plus and is currently a PhD candidate with UL. His talk will focus on improving care for patients with intracerebral haemorrhage.

Dr Hongying Chen, University Hospital Limerick

Dr Chen is a recent graduate from Trinity College Dublin; she completed her intern year in Galway and is currently a first year SHO on the BST scheme in the Department of Geriatric Medicine in University Hospital Limerick. Her main area of interest is neuro-psychiatry and she is currently pursuing a Masters degree in Applied Neuroscience with King's College London.

Short Oral Presentations

Oral Presentation 1:

Rasha A. Alshaikh, School of Pharmacy, University College Cork, Cork

"Sphingosine 1-phosphate, a potential target in neovascular retinal disease"

Rasha A. Alshaikh[1], Katie B. Ryan[1,2], Christian Waeber[1,3]

[1]School of Pharmacy, University College Cork, Cork [2]SSPC The SFI Research Centre for Pharmaceuticals, School of Pharmacy, University College Cork, Cork, Ireland [3]Department of Pharmacology and Therapeutics, University College Cork, Cork, Ireland

Worldwide, at least 2.2 billion people suffer from vision impairment; in 50% of these cases, the cause of vision loss can be treated or controlled (1). Neovascular ocular diseases are a major cause of vision impairment. Their treatment currently relies on intravitreal delivery of vascular endothelial growth factor (VEGF) blockers which neutralize VEGF, the main angiogenic mediator that initiates cascade of events responsible for progressive vision loss. Nevertheless, there is an unmet need for alternative treatment options and target diversity in addressing neovascular ocular diseases.

Sphingosine 1-phosphate (S1P) is a promising target for regulating neovascularization with potential implications in treatment of neovascular ocular diseases (2). S1P is a lipid-based mediator that acts on five G protein-coupled receptors (S1P1–5), among these, S1P1-3 receptors show predominant expression in ocular posterior chamber (2).

To investigate the role of S1P signaling in neovascularization, we tested the effects of selective S1P receptors modulators siponimod (S1P1 and S1P5 modulator) and W-146 (S1P1 antagonist) on different steps of angiogenesis using endothelial cell lines (HUVECs and Human Retinal Microvascular Endothelial Cells, HRMECs). Primary data shows that different concentrations of siponimod (100 to 10 nM) were able to inhibit endothelial cell migration. This inhibition is likely to be a result of S1P1 receptor antagonism rather than activation as similar effects were obtained by W-146 application. Neither W-146 nor siponimod increased endothelial cell proliferation when applied under normoxic conditions. However, siponimod was able to increase endothelial cell survival after hypoxia. These results suggests that siponimod can exert potential antiangiogenic action. References: (1) WHO. World report on vision. Geneva: World Health Organization, 2019. (2) Alshaikh RA, Ryan KB, Waeber C. Sphingosine 1-phosphate, a potential target in neovascular retinal disease. British Journal of Ophthalmology, Published Online: 7 May 2021.

Oral Presentation 2:

Ciara McCarthy, Department of Pharmacology and Therapeutics, University *College Cork*

"Evaluation of cytotoxic activity and chemosensitisation of acute and chronic ethanolamine treatment on oesophageal squamous cell carcinoma."

C. McCarthy[1], N.Uroz[1,2],R. Kelly-Laubscher[1], Ó.P. Barry[1]

[1]Deptartment of Pharmacology and Therapeutics, University College Cork, Cork, Ireland, [2]Univeristy of Madrid.

Oesophageal squamous cell carcinoma (OESCC) is a poor prognosis cancer. Despite treatment advances there has been limited improvement in the overall 5-year survival rate of 15% in Europe. Hence, there is a critical unmet need to design new therapeutic strategies. Ethanolamine is a biogenic amine which forms a component of membrane phospholipids and has been implicated in regulatory roles in cell division, neurotransmitter modulation and autophagy. Recently, its anticancer properties have been demonstrated in renal carcinoma in vitro (1) and in prostate cancer in vivo (2) with favourable pharmacokinetics including good oral bioavailability (2). Our study investigated both the short-term metabolic activity (using the MTT bio-reduction assay) and importantly, the long-term cytotoxic effects (using the clonogenic assay) of ethanolamine on OESCC KE-8 cells. Chronic (48 hr) ethanolamine treatment demonstrated a potent dose-dependent cytotoxic effect on KE-8 cells (IC50 = 14mM, similar to previous findings (1, 2)), chemosensitised them to the cytotoxic drugs oxaliplatin, 5-fluorouracil and decitabine and significantly (**$p<0.01$) reduced the long-term survival of KE-8 cells. Since ethanolamine is rapidly taken up into cells (2) we also investigated the effects of acute ethanolamine treatment on KE-8 cells. Interestingly, acute ethanolamine treatment (30 min, followed by a washout period) resulted in similar KE-8 cytotoxicity and chemosensitisation as well as a decrease in KE-8 cell migration. Overall, we have identified acute ethanolamine treatment as a cytotoxic and chemosensitising OESCC agent. This may aid in the design of future therapeutic regimes for treatment of this drug resistant cancer.

Oral presentation 3:

Rosie McGarvey, Centre for Cancer Research, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast,

"Investigation of the NLRP3 Inflammasome in Urothelial Cancer"

R. McGarvey[1], E. Scanlon[1], S. Maguire[1], N. McKerr[1], C. Breen[1], K. McCloskey[1], P.G Johnston[1]

[1]Centre for Cancer Research, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, 97 Lisburn Road, Belfast, BT9 7AE, Northern Ireland, UK

Bladder cancer is the 10th most prevalent cancer worldwide, with chronic inflammation being a risk factor for its development(1). The NLRP3 inflammasome is implicated in urothelial cancer (UC), with higher expression in urine of patients with high-grade tumours; however, its importance is not fully elucidated(2). This study aimed to; investigate the association between UC and NLRP3-inflammasome gene expression using publicly-available datasets and, to elucidate the effects of NLRP3-inflammasome modulators on in vitro normal urothelial (SVHUC) and UC (HT1376, T24) cell models. Differential gene expression analysis was performed comparing NLRP3-high vs NLRP3-low UC samples from the TCGA bladder cancer project. Migration, proliferation, and ELISA assays were performed investigating the effects of NLRP3 activators (10ng/mL LPS, 1mM ATP, 20μM nigericin) on inflammasome activation and functional phenotypes. The NLRP3-high cluster was associated with advanced disease ($p<0.0001$), decreased 5-year survival, and increased immune infiltrates. In ELISA assays, combining LPS/Nigericin increased IL-1β secretion, after 8 hours in T24, not SVHUC or HT1376 indicating NLPR3 activation (one-way ANOVA, $p<0.0001$, N=3). Nigericin or LPS/Nigericin combination decreased proliferation of all cell lines (one-way ANOVA, $p<0.0001$, N=3); however, migration was unaffected. In conclusion, high NLRP3-gene expression indicates advanced disease and decreased survival. NLRP3-activators reduce proliferation of UC and normal urothelial cells. This data highlights NLRP3 inflammasome signalling as an important research area for UC. Saginala et al (2020) 'Epidemiology of Bladder Cancer'. Med Sci(Basel) 8(1):15. Poli et al (2015). Expression of inflammasome-related genes in bladder cancer and their association with cytokeratin 20 messenger-RNA. Urol Oncol 33, 505.e1-7.

Short Oral Presentations

Focus on Paracetamol

Michelle Byrne, Department of Pharmacy, University Hospital Limerick

"Paracetamol: From simple analgesic to hepatotoxin. Aim: To identify potential risk factors, pharmacological mechanisms and metabolic pathways associated with the development of liver injury/failure in four inpatients following administration of IV Paracetamol at UHL."

S. NALLY[1], N. KISUKA[2], B. HAYES[1], M. BYRNE[1], A. HARNETT[1], M. SKELLY[1,2], M. ENGLISH[1]

[1]Department of Pharmacy, University Hospital Limerick, [2]Gastroenterology, University Hospital Limerick

Objectives:
The intent of this study is to: • Identify risk factors which predisposed four patients to paracetamol toxicity. • Discuss how these risk factors altered the pharmacokinetic metabolism of paracetamol. • Understand how the metabolic pathway associated with paracetamol toxicity allowed for the effective treatment with an antidote.

Method:
This study was a retrospective review of four patients diagnosed with liver injury/failure secondary to IV paracetamol administration between 2016 and 2020 at University Hospital Limerick.

Results:
The following risk factors were identified in the clinical cases as increasing the likelihood of hepatotoxicity following IV paracetamol administration: fasting, malnourishment, low body weight, administration route and overdose (exceeding recommended mg/kg). These risk factors can lead to paracetamol poisoning due to 1) depletion of hepatic glutathione stores (fasting, malnourished) or 2) oversaturation of Phase Two pathways. This alters the metabolism of paracetamol rendering the production of a more toxic metabolite (NAPQI). The treatment of paracetamol induced liver injury can be managed by replenishing glutathione stores with N-Acetylcysteine. (1)(2)

Discussion/Conclusion:
Risk factors that predispose patients to paracetamol toxicity are multifactorial. Therefore a clinical risk assessment should be complete before is commenced on IV paracetamol. Factors to be considered include: malnutrition, fasting state, weight, administration route and hepatic risk factors.

References:
(1) Lubel JS, Angus PW, Gow PJ. Accidental paracetamol poisoning. Med J Aust. 2007 Apr 2;186(7):371-2. doi: 10.5694/j.1326-5377.2007.tb00943.x. PMID: 17407437. (2) Whitcomb DC, Block GD. Association of acetaminophen hepatotoxicity with fasting and ethanol use. JAMA. 1994 Dec 21;272(23):1845-50. doi: 10.1001/jama.1994.03520230055038. PMID: 7990219.

Jennifer Kearns, Division of Geriatrics, University Hospital Limerick.

"Appropriate use of a High Risk Medication: Audit of IV Paracetamol use in a Level Four Hospital Kearns."

Kearns JO[1], Khalil M[1], Egan A[1], O'Connor M[1], Arrigan E[2], Harnett A[2]

[1]Division of Geriatrics, University Hospital Limerick, [2]Department of Pharmacy, University Hospital Limerick and Mid-West Intern Network

Background:
Intravenous Paracetamaol (IVP), widely used in Irish hospitals, is an expensive, high risk medication (HRM) when prescribed or administered incorrectly. HIQA state IVP requires risk mitigation strategies to protect patients.[1]

Aims:
Audit compliance with UHL policies, procedures, protocols and guidelines (PPPG) for IVP. Methods: 195 Kardexes were reviewed for IVP prescriptions in medical, surgical and Emergency Department (ED) wards in UHL over two days . Compliance with IVP PPPG was assessed. Clinical notes and laboratory results were reviewed for (1) IVP indication, (2) creatinine clearance calculation. Results: IVP was prescribed in 20% (n= 39). Oral (PO) or rectal routes (PR) were available in 90%. IVP was prescribed for licensed indications in 64%. Indiciation was documented in 67%. IVP was prescribed as required (prn) in 77%. Maximum daily dose (MDD) was indicated on 90% of these prescriptions. Paracetamol was inappropriately prescribed via multiple routes (PO/PR/ IV) on the same prescription in 59%. Dose adjustment per IVP PPPG was recorded in: 50% of patients with potentially reduced glutathione stores; 43% of patients with severe renal impairment (CrCl <30ml/min); one patient was < 50Kg and did not receive correct weight adjusted dose of IVP. Patient weight was not recorded on 51% of Kardexes.

Conclusions:
Non-compliance with UHL IVP PPPG is evident. Incorrect IVP use is associated with potential adverse drug events for patients and increased cost compared to oral and rectal formulations.[2] The use of IVP in 90% of patients with alternate routes available is inappropriate. Concurrent PO/PR/IV prescription may lead to prolonged use of IV route. Lack of recorded weight (51%) compromises accurate dosing and risks toxicity. An educational intervention on IVP PPPG, weight measurement importance and assessment of appropriate route is planned for prescribing staff. This will be followed by a second data collection to complete the audit cycle.

References:
1. Health Information and Quality Authority. (2019) Guide to HIQA's Medication Safety Monitoring Programme against the National Standards for Safer, Better Healthcare in acute healthcare services in 2019. [Online] Available from: https://www.hiqa.ie/sites/default/files/201901/Medication_Safety_Monitoring_Programme_Guide_2019.pdf 2. Uzoigwe C. (2015) Rapid Response: Intravenous Paracetamol: Wolf in sheep's packaging? BMJ; 351:h3705. DOI: 10.1136/bmj.h3705

Dr Ruadhan O'Laoi, Royal College of Surgeons in Ireland.

"Description of the demographics and relevant clinical indices in patients receiving n-acetylcysteine treatment for paracetamol poisoning."

R.O'Laoi[1]; C. Kennedy[1]; E. Kidney[1]

N-acetylcysteine (NAC) is an effective antidote for paracetamol poisoning, particularly when administered within 8 hours of overdose. In Ireland, the complex '3-bag/21 hour' administration protocol has remained largely unchanged for over 40 years. Modified protocols used in other Western countries, such as the '2-bag/12 hour' SNAP regimen, boast reduced rates of adverse drug reactions and shorter infusion durations without sacrificing efficacy1,2,3.

ABSTRACT SUBMISSIONS

Ellen Ahern, University Hospital Limerick

"Oral Anticoagulant Prescribing in Adult In-patients: An Audit of OAC Prescription in a University Teaching Hospital"

Ellen Ahern[1], Bushra Ali[1], Blessing Okpaje[1], Abdirahman Mohamed[1], Anastasia Saleh[1], Ahmed Gabr[1], Elaine Shanahan[1], Catherine Peters[1], Margaret O'Connor[1]

[1]University Hospital Limerick

Introduction:

In 2021, updated guidance on DOAC dosing for atrial fibrillation was published by the European Heart Rhythm Association (EHRA)

(1). Under the medicines management programme, the Health Service Executive provides guidelines on prescribing anticoagulation treatment

(2). 27% of adults were prescribed inappropriate anticoagulation dosing in the GARFIELD-AF study

(3). Methods We completed an audit of oral anti-coagulation prescribing in a university teaching hospital. A convenience sample of hospital in-patients receiving oral anticoagulants (OAC) was reviewed. The data collected included: age, OAC prescribed, dose, documentation of indication, length of treatment, if a reduced dose was prescribed and reason why, creatinine clearance and reason for co-prescribing of an antiplatelet agent.

The above guidelines were used to compare the results. Results DOACs were prescribed in 36 patients and warfarin in 4. Average age was 78. There were 6 patients who did not have an appropriate indication or duration documented. Of the patients with indication documented, 31 were on long term therapy. 18 OAC users were on a reduced dose. 6 patients had no appropriate reason documented for reduced dose prescribed. Only 9 patients had their creatinine clearance documented. 13 patients were co-prescribed an antiplatelet agent, 10 of which had a reason for co-prescription documented.

Conclusion:

Documentation of indication for prescription of OAC is essential. Indication for reduced dose and creatinine clearance were poorly documented. Interventions for improving DOAC prescribing should be explored including pharmacy input for all DOAC patients and consideration for documentation of renal parameters on the drug Kardex. References: 1. Steffel J, Collins R, Antz M, Cornu P, Desteghe L, Haeusler KG, et al. 2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation. Eur Soc Cardiol [Internet]. 2021;1–65. 2. Health Service Executive. ANTICOAGULATION PRESCRIBING TIPS [Internet]. Medicines Management Programme. 2017. Available from: www.hpra.ie 3. JP B, PN A, D A, AJ C, F C, R C, et al. GARFIELD-AF: a worldwide prospective registry of patients with atrial fibrillation at risk of stroke. Future Cardiol [Internet]. 2021 Jan;17(1):19–38.

Ali Bushra, University Hospital Limerick

"Perils of polypharmacy: A case report "

Bushra Ali[1], Ellen Ahern[1], Roz O'Byrne[1], Jennifer Condon[1], Yogeswaran Sancheyan[1], Blessing Okpaje[1], Abdi Sheikh Mohamed[1], Ahmed Gabr[1], Margaret O'Connor[1]

[1]University Hospital Limerick

Polypharmacy is an important issue in medication prescribing in older adults with multiple comorbidities. It is associated with drug interactions and adverse drug events. Here we present an interesting case outlining these issues.

Case Description:
We present the case of an 84-year-old lady with multiple comorbidities and polypharmacy (15 medications), admitted for rehabilitation after a fractured ankle requiring surgery. Background history included Osteoporosis (previous T12 fracture), Orthostatic hypotension, Hypothyroidism, Hysterectomy, Right MCA infarct, Depression, Cognitive Impairment. Bone health treatment included past bisphosphonate use (7-years); past teriparatide for 2-years, Denosumab. Other medications included: Levothyroxine, Paroxetine, Atorvastatin, Midodrine, Folic acid, Clomethiazole, Aspirin, Quinine sulphate, Nitrofurantoin prophylaxis, Pantoprazole, Dipyridamole, Paracetamol, Senna and Movicol. Issues:1)

A severe itchy scalp was her key complaint noted as an adverse effect of midodrine because of alpha 1 agonist activity on skin hair cells which led to unnecessary nizoral use. This was changed to droxidopa which is not associated with this effect and improved her symptoms. 2) Chronic kidney disease; Cockcroft-Gault creatinine clearance was 20. Many of her medications were contraindicated including bisphosphonates, teriparatide, midodrine, nitrofurantoin. Cautious use of denosumab was recommended due to increased risk of hypocalcemia with replacement of 1,25-hydroxy-choleciferol, Clomethiazole was noted to have increased risk of confusion and falls, her presenting complaint. Paracetamol analgesia was appropriately adjusted.

Discussion:
Polypharmacy is a major issue in older adult prescribing. Physiological changes with ageing impact pharmacokinetics and pharmacodynamics increasing adverse reactions. Renal or hepatic impairment complicate matters. Drug-Drug interactions nail the coffin as one prescribes for multiple indications.

Osama Ali, Beaumont Hospital Geriatric Department

"Appropriateness of prescribing and monitoring of enteral electrolyte replacement in Beaumont Hospital"

Audit Lead: Prof. Alan Martin[1]
Audit Authors: Osama Ali[1], William Smith[1], Claire Stenson[1]

[1]Beaumont Hospital Geriatric Department

Background/rationale for audit:

Electrolytes are essential for basic metabolic function (e.g. generating and conducting action potentials in the nerves and muscles). Electrolyte imbalance, either high or low, can lead to the disruption in physiologic function and can have life-threatening. Therefore, electrolyte replacement and monitoring is very important in clinical care. Enteral electrolyte replacement is very common in the inpatient setting, but poorly monitored. Commonly prescribed oral electrolytes are potassium, phosphate and magnesium. Prolonged courses and under-monitoring can adversely affect patient outcomes and prolong hospital stay. [1, 2, 3]

Aim & Objectives:

1. Assess appropriateness of oral electrolyte replacement prescribing

2. Check compliance with prescribing guidelines

3. Assess electrolyte monitoring during replacement therapy

Sample: Random sampling of inpatients in Beaumont Hospital including medical and surgical wards Standards/guidelines/evidence base:

1. PPCC-GEN-1: Beaumont Hospital Guideline on: Prevention and Treatment of Refeeding Syndrome.

2. Prescribing Guidelines for HYPO-Electrolyte Disturbances in Adults. Fluid and Electrolyte Guideline Working Party. Queensland Government.

3. Best Practice Methodology: Prospective review of the inpatient medical and surgical population. The patient's kardexes and clinical lab results were reviewed to determine if appropriate electrolyte replacement is commenced, monitored and ceased based on the clinical electrolyte results. Also, a medication review was carried out to review if prescribed medications could have contributed to any electrolyte disturbance. Finally, if patient's prescribed medication is identified as a possible contributor, was the prescription modified to help correct any disturbance

Results/findings:

During the course of our audit we deemed it useful to document the type of electrolyte prescribed. We documented this in 38 forms (n=53). Of the electrolytes prescribed potassium was the most commonly prescribed electrolyte 18 out of 38 (47%), phosphate was second with 12 and magnesium third with 8. No other electrolyte types were captured in this audit. On review of our results the electrolyte was prescribed correctly as per the kardex rules to include name, signature, MCN, route, frequency in 30 cases. (30/53 = 57%). Commonly omitted areas documented in our audit were signature and MCN. Prescribers used correct patient identity on the Kardex page in 85% of cases (45/53). IV replacement was indicated in 6/53 (11.3%) of the patients. It is unclear with the exception of 1 patient if IV replacement was commenced, as this information was not within the scope of our audit. A

start date was documented in all cases however a stop date was only noted in 17/53 cases. (32%). All patients with the exception of 1 had up to date electrolyte serum levels prior to commencing on oral replacement. Daily electrolyte levels used to guide treatment were only carried out on 62.2% of patients (33/53). Following the ceasing of the electrolyte, levels were checked in 11/53 patients and not checked in 6/53, however of note this data was not captured in 36/53 (67.9%) of cases in our audit as it wasn't applicable due to ongoing prescription. Regarding the appropriateness of stopping the electrolyte this did not happen in 11/53 (20%) cases and the electrolyte was either ongoing or had continued after the return to normal serum electrolyte levels on labs. The most prolonged courses after electrolyte levels normalised were 11 days, 6 days and 5 days. In relation to the reason for electrolyte imbalances 18/53 (40%) patients were noted to have a drug/s possibly contributing to the abnormality. Of the cases captured 9/53 (17%) patients were noted to have interactions with their prescribed drugs and the electrolyte prescribed. Where the above was noted only 1 patient had their prescription modified owing to either interaction or contribution to abnormality. The remaining 34 patients had no interaction or contribution noted in the audit.

Conclusions:
Oral potassium is the most frequently prescribed supplement in Beaumont hospital. Overall, poor compliance to prescribing rules were observed in oral electrolyte replacement especially prescriber signature and MCN. Although adequate serum electrolyte monitoring was performed in most of the patients, oral electrolyte prescription wasn't stopped in 20% of the cases which may lead to adverse drug reaction due to over correction. Improvement is required in clinical practise to observe drug-drug interaction and adverse drug reaction. If potential drug is contributing to the electrolyte imbalance and clinician deems it appropriate not to modify it, clear reason should be documented and further appropriate measure should be taken to avoid adverse patient outcome. Recommendations and action plan: Improve compliance of prescribing and sufficient monitoring for patients receiving enteral electrolyte replacement. Provide audit results and conclusions to inpatient teams along with education re correct prescribing and monitoring of electrolyte replacement therapy Increase awareness re. in-hospital guidelines of electrolyte replacement via NCHD teaching sessions and Beaumont newsletter References: 1. PPCC-GEN-1: Beaumont Hospital Guideline on: Prevention and treatment of Refeeding Syndrome 2. Zaloga GP, K.R, Bernards WC, Layons AJ, Fluids and Electrolytes 3. Polderman et al. J. Neurology 2001 May; 94(5): 697-705

Rasha A. Alshaikh, School of Pharmacy, University College Cork, Cork

"Sphingosine 1-phosphate, a potential target in neovascular retinal disease"

Rasha A. Alshaikh[1], Katie B. Ryan[1,2], Christian Waeber[1,3]

[1]School of Pharmacy, University College Cork, Cork [2]SSPC The SFI Research Centre for Pharmaceuticals, School of Pharmacy, University College Cork, Cork, Ireland [3]Department of Pharmacology and Therapeutics, University College Cork, Cork, Ireland

Worldwide, at least 2.2 billion people suffer from vision impairment; in 50% of these cases, the cause of vision loss can be treated or controlled (1). Neovascular ocular diseases are a major cause of vision impairment. Their treatment currently relies on intravitreal delivery of vascular endothelial growth factor (VEGF) blockers which neutralize VEGF, the main angiogenic mediator that initiates cascade of events responsible for progressive vision loss. Nevertheless, there is an unmet need for alternative treatment options and target diversity in addressing neovascular ocular diseases.

Sphingosine 1-phosphate (S1P) is a promising target for regulating neovascularization with potential implications in treatment of neovascular ocular diseases (2). S1P is a lipid-based mediator that acts on five G protein-coupled receptors (S1P1–5), among these, S1P1-3 receptors show predominant expression in ocular posterior chamber (2).

To investigate the role of S1P signaling in neovascularization, we tested the effects of selective S1P receptors modulators siponimod (S1P1 and S1P5 modulator) and W-146 (S1P1 antagonist) on different steps of angiogenesis using endothelial cell lines (HUVECs and Human Retinal Microvascular Endothelial Cells, HRMECs). Primary data shows that different concentrations of siponimod (100 to 10 nM) were able to inhibit endothelial cell migration. This inhibition is likely to be a result of S1P1 receptor antagonism rather than activation as similar effects were obtained by W-146 application. Neither W-146 nor siponimod increased endothelial cell proliferation when applied under normoxic conditions. However, siponimod was able to increase endothelial cell survival after hypoxia. These results suggests that siponimod can exert potential antiangiogenic action. References: (1) WHO. World report on vision. Geneva: World Health Organization, 2019. (2) Alshaikh RA, Ryan KB, Waeber C. Sphingosine 1-phosphate, a potential target in neovascular retinal disease. British Journal of Ophthalmology, Published Online: 7 May 2021.

Anne Harnett, University of Limerick and University of Limerick Hospital Group

"Evaluation of Medication risk mitigation strategies at ULHG"

Anne Harnett [12], Susan Stack[2], Michelle English[2]

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Background:
A key component of the Medication safety programme of the University of Limerick Group of Hospitals (ULHG) is the implementation of medication safety initiatives (MSI) formulated with cognisance of either • National and International recommendations relating to medication safety • Outcomes of review of locally reported medication safety incidents or audit findings which lead to consequent risk-mitigating recommendations

Aim:
To evaluate, according to an internationally recognised hierarchy of effectiveness of risk reduction strategies, MSI implemented at ULHG in order to establish the percentage of initiatives categorised in the High Leverage most effective category.

Method:
MSI implemented at ULHG between January 2018 and September 2021 were examined and categorised according to the hierarchy of effectiveness of risk reduction strategies developed by Institute of Safe Medication Practice (ISMP). This hierarchy separates two broad categories. described as person-based or system-based. These broad categories are further subdivided according to evaluation of both leverage and effectiveness • Leverage- low, medium or high • Effectiveness – least, moderate or most effective Results Of 31 MSIs reviewed, 42% (13/31) were person-based, while 58% (18/31) were system-based. 32%(10/31) of the system-based MSI were rated to be high leverage and most effective.

Discussion:
Categorisation of MSI according to whether an initiative is system-based or person-based, with further sub-categorisation according to levels of leverage and effectiveness is a useful review exercise which can inform prioritisation of future initiatives as well as optimisation of available resource.

Siobhan Barrett, Department of Pharmacy, University Hospital Limerick

"Cytochrome P450 3A4 - A Tale of Two Substrates"

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Clarithromycin, a potent CYP3A4 inhibitor and a CYP3A4 substrate, is a macrolide antibiotic included in many hospital antimicrobial guidelines for treatment of Community Acquired Pneumonia (CAP). Carbamazepine, a CYP3A4 substrate, is prescribed for its antiepileptic, neurotropic and psychotropic effects (1). A clinically significant drug-drug interaction can be expected when these agents are co-prescribed, through clarithromycin's inhibition of the CYP3A4 mediated metabolism of carbamazepine (2), (3).

We present two patients, admitted to hospital, with pre-existing prescriptions for carbamazepine. Clarithromycin (with beta-lactam antibiotics) was commenced on admission for respiratory tract indications for both patients. Patient A was treated for Infective Exacerbation of Chronic Obstructive Pulmonary Disease (COPD). Patient B was treated for CAP. Both patients developed new onset neurological symptoms within three days of commencing clarithromycin.

Patient A became unresponsive, developed jerking movements and was treated for possible new seizure activity, with the addition of levetiracetam. CT brain was performed. Patient B developed tremors, shaking of the hands and jerking movements. Neurological effects are known symptoms of carbamazepine toxicity (1), (2), (3).

Carbamazepine levels, on request, were noted to be in the toxic range for both patients (109micromol/L and 104micromol/L respectively. Therapeutic range is 17 to 51micromol/L) (4). Carbamazepine toxicity was established as the cause of both patients' neurological symptoms. The potent CYP3A4 inhibitory properties of clarithromycin are well documented. Definitive indication for clarithromycin use should be established prior to prescribing. Awareness of potential drug-drug interactions is essential to prevent unwanted adverse effects due to decreased metabolism of concomitant CYP3A4 substrates.

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"Exploratory analysis of troponin as a biomarker of acute ischaemic stroke subtypes in a subset group of patients recruited to the MiND study"

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Abstract Introduction:
Stroke is a major common cause of acquired disability and death worldwide. Atrial dysfunction or cardiomyopathy, defined by the presence of specific serum biomarkers, ECG findings, or echocardiographic findings, increase the risk of atrial fibrillation, which has been implicated as a key risk factor for ischaemic stroke.1 There is now growing body of evidence which suggest that early positive troponin after ischaemic stroke may be independently associated with a cardiac embolic source.2 miRNA as Novel Diagnostic biomarker (MiND) is a current Irish-led research study whose aim is to discover a unique highly diagnostic and prognostic biomarker expressed in acute ischaemic stroke.

Aim:
We hypothesized that early elevated troponin is a predictor of cardiac source of embolus in patients with Embolic stroke of unknown source (ESUS) as compared with non-cardioembolic stroke (NCE). Methodology: Data was retrospectively extracted from patients recruited to the MiND study with confirmed diagnosis of acute ischaemic stroke within 12 hours of symptoms onset having also undergone high-sensitivity troponin testing from July 2019 to July 2021 and an interim analysis carried out. Statistical analysis was carried out using STATA/SE, version 16.0.

Results:
We identified 43 patients who had troponin performed within 12 hours of symptoms onset. Stroke subtypes were classified as per ESUS criteria. Twenty-two patients were identified as having cardioembolic stroke (CE), 12 as non-cardioembolic stroke (NCE) and 9 as Embolic stroke of unknown source (ESUS). The mean age for each group was 77.5 (±9.2), 66.4 (±13.1) and 62 (±11.4) years, respectively. The rate of troponin positivity for each group was 55% (12/22), 33% (4/12) and 0% (0/9), respectively. The unadjusted logistic analysis revealed a positive association between CE stroke subtype and elevated troponin (OR 5.1, 95% CI 1.29-20.17, p = 0.020) and a negative association between NCE stroke subtype and elevated troponin (OR 0.79, 95% CI 0.20-3.21, p = 0.744). Logistic regression analysis reveals a perfect association between normal troponin level and ESUS stroke subtype. Conclusions: Our analysis reveals that early positive troponin after ischaemic stroke is a strong predictor of CE stroke subtype but not of ESUS stroke subtype.

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Dr Teresa Barbosa, School of Pharmacy University college Cork

"A Clinical and Cost Analysis of Medication Reconciliation by Clinical Pharmacists on Hospital Discharge"

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As patients transition between healthcare providers and settings, discrepancies and miscommunication in medical records are common and lead to serious medication errors and subsequent adverse events.(1) Despite well-established medication reconciliation processes at the point of hospital admission, clinical pharmacists' do not routinely undertake medication reconciliation at discharge thus the impact of pharmacists' involvement in medication reconciliation at this transition point was assessed. This prospective observational study was conducted on adult patients meeting inclusion criteria on a number of medical wards, during a six-week period May - June 2021. The prevalence of non-reconciliations were evaluated while their clinical significance was analysed by an expert peer review panel using a validated scoring tool. 106 patients were included with medication non-reconciliations identified in 86(81.1%) patients involving 284(22.4%) of 1266 medications. Of these 48.6% were 'prescription non-reconciliations' and 51.4% 'communication non-reconciliations'. The peer review panel deemed 172(60.8%) and 6(2.1%) non-reconciliations to have a 'moderate' and 'severe' potential for harm respectively while 145(51.1%) non-reconciliations were considered as having a 'moderate' potential for hospital readmission and 9 (3.2%) deemed as having a 'high' potential. In relation to the likelihood to require clarity in the community, 181(63.7%) and 13(4.6%) were deemed 'likely' and as 'requiring clarification' respectively. An estimated cost-avoidance of €29,792.57 was found. Incomplete and erroneous discharge prescriptions are common with pharmacists' playing an effective and important role in identifying non-reconciliations and subsequently reducing potential patient harm and hospital readmissions, bridging the communication gap with primary care while also having a significant beneficial financial impact.

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Róisín Cassidy, Department of Pharmacology and Therapeutics, University College Cork, Cork, Ireland

"Valproic acid can enhance autophagy and sensitivity to 5-fluorouracil but not oxaliplatin in oesophageal cancer cell lines."

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Oesophageal cancer is a devastating disease with European five-year survival at less than 18%. Standard chemotherapy involves a combination of 5-fluorouracil (5-FU) and oxaliplatin. Loss of apoptosis and/or modulation of autophagy has been associated with drug resistance. Histone deacetylase (HDAC) inhibitors have emerged as potential chemo-sensitiser's due to reported effects on apoptosis and autophagy. We examined the effects of the HDAC inhibitor, valproic acid (VPA) on two oesophageal squamous cancer cell lines (KE-8 and KYSE-450). Treatment with VPA treatment alone (1-1.5mM) induced autophagic flux in both cell lines as demonstrated by autophagosome staining with CytoID in the presence of chloroquine and quantification by flow cytometry. Treatment with 5-FU (10-12.5μM) also induced autophagy in both cell lines and this was further elevated in the presence of VPA (1-1.5mM). Co-treatment with VPA also enhanced the cytotoxicity of 5-FU in both cell lines, demonstrated by clonogenic assays. Apoptotic morphology was present in KE8 cells treated with 5-FU but not in KYSE450. It is possible that a cytotoxic form of autophagy or excessive autophagy contributed to this enhanced response, and this will be evaluated with an ATG7 knockdown. Oxaliplatin (750nM-1μM) also induced autophagy in both cell lines. However, this was either unaffected or inhibited by VPA. In contrast to 5-FU, the cytotoxicity of oxaliplatin was significantly reduced by VPA in both cell lines. This data indicates the potential for chemo-sensitisation with VPA is highly dependent upon the specific cytotoxic agent in the combination and may be associated with effects on autophagy.

Jennifer Kearns, Division of Geriatrics, University Hospital Limerick.

"Appropriate use of a High Risk Medication: Audit of IV Paracetamol use in a Level Four Hospital."

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Background:
Intravenous Paracetamaol (IVP), widely used in Irish hospitals, is an expensive, high risk medication (HRM) when prescribed or administered incorrectly. HIQA state IVP requires risk mitigation strategies to protect patients.[1]

Aims:
Audit compliance with UHL policies, procedures, protocols and guidelines (PPPG) for IVP. Methods: 195 Kardexes were reviewed for IVP prescriptions in medical, surgical and Emergency Department (ED) wards in UHL over two days . Compliance with IVP PPPG was assessed. Clinical notes and laboratory results were reviewed for (1) IVP indication, (2) creatinine clearance calculation. Results: IVP was prescribed in 20% (n= 39). Oral (PO) or rectal routes (PR) were available in 90%. IVP was prescribed for licensed indications in 64%. Indiciation was documented in 67%. IVP was prescribed as required (prn) in 77%. Maximum daily dose (MDD) was indicated on 90% of these prescriptions. Paracetamol was inappropriately prescribed via multiple routes (PO/PR/ IV) on the same prescription in 59%. Dose adjustment per IVP PPPG was recorded in: 50% of patients with potentially reduced glutathione stores; 43% of patients with severe renal impairment (CrCl <30ml/min); one patient was < 50Kg and did not receive correct weight adjusted dose of IVP. Patient weight was not recorded on 51% of Kardexes.

Conclusions:
Non-compliance with UHL IVP PPPG is evident. Incorrect IVP use is associated with potential adverse drug events for patients and increased cost compared to oral and rectal formulations.[2] The use of IVP in 90% of patients with alternate routes available is inappropriate. Concurrent PO/PR/IV prescription may lead to prolonged use of IV route. Lack of recorded weight (51%) compromises accurate dosing and risks toxicity. An educational intervention on IVP PPPG, weight measurement importance and assessment of appropriate route is planned for prescribing staff. This will be followed by a second data collection to complete the audit cycle.

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Emma Field, University Hospital Limerick

"Meropenem focused Antimicrobial Stewardship Ward Rounds , An Intervention to Improve Meropenem Prescribing"

Emma Field[1]

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Background:
The HSE policy on restricted antimicrobial agents , highlights the requirement for restriction of the carbapenem group of antimicrobials. Complete restriction of meropenem is not currently implemented in UHL. It is recommended that meropenem is only prescribed following consultation with the Micro/ID teams. Since Oct 2015, all prescriptions of meropenem are followed by the Antimicrobial Pharmacists. Any prescription which was not pre-approved is highlighted to the clinical team by the use of a specific "meropenem alert sticker" placed in the clinical notes, reminding prescribers on the requirement to discuss further. The consumption of meropenem is expressed as DDD/100BDU (defined daily doses per 100 bed days used). In 2019 UHL DDD/100BDU for meropenem was 3.12 vs 2.88 for national tertiary hospitals. In 2020 UHL DDD/100BDU for meropenem was 2.14 vs 2.51 for national tertiary hospitals.

Methods:
To address ongoing non-compliance, a weekly meropenem specific ward round was introduced in June 2019, focusing on 1)meropenem prescriptions that were not pre-approved by Microbiology/ID before prescribing 2)review of all ongoing prescriptions of meropenem with formal documented recommendations on de-escalation and duration of treatment

Results:
Evaluation of this initiative after 6 months showed an improvement in compliance with the requirement for pre-authorisation of meropenem from 62% in May 2019 (pre-intervention) to 78% in December 2019. Now in Q2 2021 compliance was 83% (>KPI of 80%) Conclusion :This intervention showed preliminary positive results with an increase in compliance over a 6 month period. Two years on, results remain positive.

Eva Fitzgerald, Senior Clinical Pharmacist Paediatrics, Pharmacy Department, University Hospital Limerick

"Quality improvement project to improve prescription writing and medicine administration documentation at Paediatric Unit UHL"

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Abstract:

i) the problem being addressed in the study:

Deficiencies existed in the Medication Prescribing and Administration Record (MPAR) design for paediatric patients at UHL. These deficiencies were known from the results of prescribing audits including national Nursing Metric Audits, from incident reports and from feedback received from nurses, pharmacists and non-consultant hospital doctors at UHL. In 2016 the HSE's (Health Service Executive) published a national template for MPARs (for adults) and around the same time Children's Health Ireland (CHI) finalised the design of their MPAR. Under the governance of the UL Hospitals Group Drug and Therapeutics committee, the Paediatric Medication Safety Committee (PMSC) formed a working group to address the deficiencies and update the paediatric MPAR at UHL. The problems with the MPAR included not having a space to prescribe the 'frequency' and having an anticoagulation section titled 'Adult' with prescribing guidance for adult patients.

ii) how the study was performed:

A gap analysis of the current MPAR and the national template was completed and discrepancies reviewed by the PMSC. Further discussion at PMSC resulted in a decision to review the CHI MPAR as a starting draft document for the update UHL MPAR. Subsequent drafts were reviewed by nurses, pharmacists and prescribers and their feedback informed the next draft. The final draft was subject to a pilot study in paediatric clinical areas. Feedback from the pilot study informed the final design.

iii) the salient results

The adapted national CHI MPAR was implemented in all paediatric clinical areas. An audit of prescription writing and medicine administration record was conducted and show improvement e.g. the 'frequency' part of the prescription was completed in 100% of prescriptions; this had been at 0% compliance before the update. iv) what the authors conclude from the results The updating of the MPAR for paediatric patients has improved prescription writing and satisfaction with the update is high particularly among prescribers who use the MPAR both while working in CHI and locally at UHL. v) references - indicated in the text as (1), (2) etc. and cited at end of abstract 1. HSE National Medication Safety Programme published an MPAR Template in March 2017 2. CHI MPAR 3. Healthcare Records Management, HSE http://www.hse.ie/healthcarerecords 4. IMSN Allergies http://www.imsn.ie/all-news/18-briefing-documents/62-allergies 5. HPSC Report Antimicrobial Stewardship in Irish Hospitals 2009

Michelle Fitzsimons, Department of Pharmacy University Hospital Limerick

"Baseline Audit of Vancomycin Prescriptions in Intermittent Haemodialysis Patients at University Hospital Limerick (UHL)"

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The purpose of the audit was to establish if vancomycin is prescribed as per UHL guideline and if the guideline dosing achieves target blood drug levels. The results would be used to update the current guideline. A retrospective audit of vancomycin prescriptions for haemodialysis patients in UHL over four months in 2018-2019 was conducted. Patients were identified by vancomycin levels linked to the dialysis unit. Chart number, patient pre-dialysis weight, date and time of dose, date and time of level and whether prescribed in the inpatient and dialysis kardex was recorded. Excel was used to analyse data. Loading and maintenance doses were analysed separately. Ethics approval was obtained. Results: 28% doses reached target range after one loading dose. Time to first target blood level ranged from 0.5 day to 6.5 days 64% of levels taken 72 hours after dose were sub therapeutic. 15% complied with prescription requirements Loading doses and levels were variable and there was no correlation between the loading dose and level achieved. The maintenance dosing achieves target range in the majority of patients if vancomycin is dosed at least three times weekly. Dosing at intervals greater than 72 hours may result in sub therapeutic levels. Compliance with the prescription writing requirements was poor. The audit highlight the need to give guidance on managing dosing in the initial stages of treatment and to advise that the guide is only suitable for thrice weekly dialysis. Compliance with prescription writing was poor and this could be addressed at induction.

References

1. Administration of Intravenous Vancomycin in Haemodialysis patients (UL Hospital Group)

Ahmed Gabr, St. James's Hospital, Dublin, Ireland and University Limerick Hospital Group

"Tuberculosis Rising in the Era of Tumour Necrosis Factor alpha Blockade: An Irish Experience"

Ahmed Gabr[1,2], Khalid E. El Kholy[1], Cormac Kennedy[1,3], Kevin Brown[1], Sarah Jackson[4], Bushra Ali[2], Michael Barry[1,3,4], Joseph Keane[1], Mary O'Meara[1,5]

[1]St. James's Hospital, Dublin, Ireland, [2]University Limerick Hospital Group, [3]Trinity College Dublin, [4]National Centre for Pharmaco-Economics, [5]Dr. Steevens Hospital, Dublin

Aims:
Despite the overall decreasing incidence of Tuberculosis (TB) infection in Ireland, TB cases associated with Tumour Necrosis Factor-alpha (TNF-α) antagonists are increasing. We aimed to report the incidence of anti-TNF-α associated TB cases on a national level over a 10-year-period and highlight the overall prescribing frequency of these agents.

Methods:
Data on TB incidence and prescribing frequency of anti-TNF-α agents were extracted from the Health Protection Surveillance Centre (HPSC) and the Primary Care Reimbursement Service (PCRS) annual reports, respectively. Results The incidence of TB cases where anti-TNF-α usage was reported as a risk factor has increased five and half fold from 2008 (6.4 events/1000 cases) to 2018 (34.9 events/1000 cases). This was positively correlated with the prescribing frequency of anti-TNF-α which has increased three and half fold during the same time period [r (11) = .81, p = .002].

Discussion:
There is a decreasing incidence of TB globally. The risk of TB in patients on anti-TNF-α is well established. Our study demonstrated the increasing utilisation of anti-TNF-α agents in Ireland and a correlated increase in TB cases in those who are on anti-TNF-α. This trend likely reflects the increasing risk of TB in these patients. Mitigation strategies are required which may include agents with similar efficacy but a lower risk of TB.

Ahmed Gabr St. James' Hospital and Trinity College Dublin

"Implementation of an Intracerebral Cerebral Haemorrhage Care Bundles"

Ahmed Gabr, Nora Cunningham, Cormac Kennedy, Abdirahman Mohamed, Blessing Okpaje, Anastasia Saleh, Aoife Leahy, Khalid El-Kholy, Ida Carrol, Shiji Paulose, Norma Daly, Anne Harnett, Emily Buckley, Patrick Kiely, John McManus, Catherine Peters,Collin Quinn, Elaine Shanahan, Declan Lyons, Mike Watts, Denis O'Keefe, Rose Galvin, Sean Murphy, Margaret O'Connor

Background:
Mortality for Intracerebral haemorrhage (ICH) is 31% (INAS, 2019). An ICH care bundle focusing on acute anticoagulation reversal, blood pressure lowering, and neurosurgical care pathway was associated with improved survival. The aim of this study was to determine the feasibility and outcomes of implementation of a bundle of care. Translating evidence-based medicine into clinical practice is well recognized to be a challenging process

Methods:
An ICH care bundle was developed using an iterative process involving expert stakeholder feedback and review of the evidence-based literature. A pre-and-post quasi-experimental research design was employed to evaluate this intervention. Baseline data were collected before implementation (January 2016-June 2018). Implementation took place in a staged manner with multiple PDSA cycles (June 2018 to January 2021). Data on compliance, process measures outcomes were collected.

Results:
Systolic blood pressure in the first 24 hours and anticoagulant reversal were significantly better controlled in the post-implementation group (X^2 (1, N=91) = 5.34, p=0.02), (X^2 (1, N=25) = 5.85, p=0.016), respectively. The overall DNAR orders were significantly lower in the post-implementation group (X^2 (1, N=25) = 5.85, p=0.029). However, DNAR status did not significantly differ when accounting for low GCS as a surrogate measure for poor prognosis (X^2 (1, N=34) = 0.00, p=0.966). Modified Rankin Scale on discharge did not differ significantly pre-and-post-implementation (z=-0.075, p=0.94). A greater proportion of patients survived in the post-implementation group; however, this was not statistically significant (X^2 (1, N=133) = 0.77, p=0.38). The length of stay significantly increased post implementation.

Conclusion:
An ICH care bundle was developed based on expert stakeholder feedback. The feasibility of implementing this bundle of care was demonstrated in a real-world clinical practice setting. A cluster-randomized trial or a large registry study is the next step to evaluate the clinical impact of this care bundle on patient outcomes.

Louise Hayes, University Hospital Limerick

"Audit on the prescription and administration of Parkinson's disease medication on admission to hospital"

Louise Hayes[1], Elaine Arrigan[1], Margaret Richardson[1], Anne Barry[1], Emma Cagney[1]

[1]University Hospital Limerick

The National Institute for Health and Care Excellence (NICE) recommends that Parkinson's Disease (PD) patients who are hospitalised take levodopa within 30 minutes of their individually prescribed administration time (1). In some cases this may require self-medication (2). Serious complications can develop if levodopa is not taken on time that can lead to increased care needs and increased length of stay in hospital (1). The aim is to evaluate whether the prescription and administration of PD medicines in UHL complies with best practice recommendations.

This baseline audit was carried out over a 12 week period in 2021. Data were collected on 50 PD admissions. Data relating to PD medicines prescribed for the management of motor symptoms was collected. The following information was recorded:

• Unintentional discrepancies on the admission prescription following a medication reconciliation (MR)

• The number of delayed or omitted doses of PD medicines since admission

• The number of patients that administered their own PD medicines

Unintentional discrepancies on the admission prescription were associated with 34% (n=138) of PD medicines reviewed. 80% (n=50) of patients were affected by a delay or omission of PD medicines since admission to hospital. 36% (n=296) of doses of levodopa PD medicines were delayed or omitted. 20% (n=50) of admissions took their own PD medicines while in hospital. Greater emphasis should be placed on accurately prescribing and administering PD medicines in the hospital setting. Consideration should be given to introducing a Self-administration Policy for PD patients.

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"Understanding the Social Transmission of Visceral Pain; a new rodent model to assess pain-induced trauma"

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Psychological and physical trauma can induce significant pathological alterations, and lead to the manifestation of post-traumatic stress disorder (PTSD). Moreover, secondary traumatic stress (STS) is a trauma-related condition that develops after witnessing another individual or group undergo a severe or life-altering event. These trauma-related disorders are often concomitant with comorbidities such as anxiety, depression, pain, and gastrointestinal disturbances. Visceral pain is a specific type of pain that originates from the internal organs of the body, and despite its widespread prevalence, it remains poorly understood. To develop a more comprehensive view of the linkage between visceral pain and STS, we established an observation paradigm that allowed us to assess the impact of STS on visceral pain sensitivity. We aim to understand if the observation of visceral pain behaviours induces visceral hypersensitivity.

Briefly, we utilised the well-established colorectal distension (CRD) paradigm to induce visceral pain behaviours in a stimulus rodent whilst the STS rodent observed. 24 hours post observation, the visceral sensitivity of the STS rodent is assessed using CRD. The STS rats were found to have a significantly lower visceral pain threshold than control rats, indicating visceral allodynia. Furthermore, these animals also showed a higher number of total pain behaviours indicative of visceral hypersensitivity. These results suggest that observing another animal in distress and pain elicits a secondary traumatic stress type phenotype. Given that these psychiatric disorders are prevalent, and rising worldwide, we need to gain a better understanding of the underlying mechanisms to aid future development of effective treatments.

Kyle Malone, Department of Pharmacology & Therapeutics, School of Pharmacy, University College Cork, Ireland

"Changes in Treg Frequency and Function in Ischaemic Stroke Patients"

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Introduction: Stroke is a major cause of morbidity and mortality worldwide. While many parts of the immune system contribute to stroke damage, a lymphocyte subset termed regulatory T cells (or "Tregs") have been shown to provide neuroprotection. To date, however, the impact of brain ischaemia on Tregs in stroke patients remains understudied. The aim of this study was to comprehensively quantify Treg frequency in both the acute and subacute post-ischaemic period. Methods: Blood was collected from stroke patients (n = 12) at 24 hours (T1) and one week (T2) post-brain ischaemia, and age-matched controls (n = 9). Flow cytometry was used to quantify circulating Treg (CD4+CD127-CD25+FoxP3+ cells) frequency, naïve (CD45RA+), memory (CD45RA-), and proliferating (Ki67+) subsets. The expression of functional markers of suppression (CD39, CTLA-4, PD-1) by these subsets was then quantified. Results: Stroke increased circulating Treg frequency compared to control, specifically due to an increase in FoxP3 expression. Subset analysis revealed proliferating Tregs (pTregs) were elevated at 24 hours post-ischaemia. Enhanced expression of both PD-1 and CTLA-4 by pTregs was also observed. A reduction in overall Treg frequency and circulating pTreg CTLA4+/PD-1+ frequency occurred by 7 days post-ischaemia. Conclusions: An increased circulating Treg frequency is observed in the acute post-stroke period, specifically due to a rise in pTregs. Enhanced expression of functional markers of suppression (CTLA-4, PD-1) among pTregs also occurs. However, by 7 days post-ischaemia, a decrease in both Treg frequency and function is noted. Future post-stroke Treg-targeted immunotherapies may therefore need to exploit this subacute period.

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"Investigation of premature cellular senescence in Pre-eclampsia and Intrauterine Growth restriction"

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Introduction:
Premature aging of the placenta is associated with placental insufficiency, which reduces its functional capacity and leads to abnormal pregnancy outcomes. To investigate how senescence contributes to placental ageing, both the senescence associated secretory phenotype (SASP) and defined markers of cellular senescence were determined in both obstetric complications.

Methods:
Maternal plasma and placental samples were taken at term from nulliparous women with pre-eclampsia (PE) (n=13), intra-uterine growth restriction (IUGR) (n=13) and age-matched healthy pregnancies (n=20). SASP panel of cytokines were evaluated in maternal plasma by multiplex ELISA assay. Placental absolute telomere length and senescence gene analysis was performed by RTqPCR. Statistical analysis was performed using Stata 14.2 and GraphPad Prism 8®.

Result:
Plasma IL-6 levels was significantly increased when in PE only compared to controls (0.54 pg/ml ± 0.271 v 0.3 pg/ml ± 0.102; p=0.017). Adjusting for variables, IUGR>3rd centile had a 1.522kbp (95% CI:-6.852, 3.807) shorter telomere length; whereas PE-+IUGR 1.675kbp (95% CI: -3.527, 6.878) and PE 4.882kbp (95% CI: -0.391, 10.155) had longer telomere lengths when compared to controls, results didn't reach significance. Quantification of placental mRNA expression of senescence markers showed a significant increase in CHEK1 expression in PE (p=0.007) and IUGR >3rd centile (p<0.001) while a significant decrease in TBX2(p=0.016) and PCNA(p=0.037) expression was evident only in IUGR >3rd centile when compared to controls.

Conclusion:
While the hallmarks of premature senescence are evident in PE and IUGR there appear to be different senescent phenotypes and cellular regulators involved in mediating the process in each obstetric complication.

Martina Mannion, Mid West Intern Network, University of Limerick Hospital Group

"Drug interactions, toxicity & stroke mimic: the complexities of prescribing"

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Introduction:
Ischemic stroke is a medical emergency. Mimics of stroke represent up to 30% of stroke presentations. Drug adverse events may mimic stroke and lead to misdiagnosis and harmful treatment. These need to be considered as part of the overall differential diagnosis of stroke.

Case Presentation:
We present the case of a 75-year old woman who was transferred to our stroke pathway from a peripheral hospital with subacute onset of dysarthria, ataxia and delirium. Her medical history included hypertension, atrial fibrillation, heart failure and trigeminal neuralgia. Medications included: bisoprolol 2.5 mg OD, apixaban 5mg BD, atorvastatin 20mg and carbamazepine 600mg BD Examination showed bilateral upper limb ataxia with direction-changing horizontal and vertical nystagmus and drowsiness consistent with a central neurological cause. The unclear time of onset of symptoms beyond 24 hours meant that this patient was outside the window for hyper-acute stroke treatment.

Discussion:
Initial concern was sub-therapeutic anti-coagulation due to cytochrome-3A4 interactions between carbamazepine (inducer) and apixaban leading to stroke. MRI brain was however normal. This patient had been prescribed carbamazepine for trigeminal neuralgia however she was taking it on a PRN basis only pre admission. When prescribed regularly over a period of 3 days she rapidly developed toxicity. This was a clinical diagnosis. Carbamazepine levels were taken and subsequently found to be elevated. Symptoms and signs resolved with discontinuation of the offending drug.

Abdirahman Sheikh Mohamed

"Evaluation of diabetes in a Cohort of Frail Older adults"

Dr Abdirahman Sheikh Mohamed; Dr Siobhan McGettigan; Dr Wed Mustafa; Dr Ahmed Gabr; Prof Margaret O'Connor; Dr Pillay; Dr Mary Jane Brassill

Aim:
Presence of frailty has great impact on both prognosis and treatment of diabetes. The aim of this study was to identify the prevalence of diabetes in a cohort of frail older adults who attended Tipperary University Hospital (TUH), and explore the relationship between frailty and diabetes in this cohort.

Method:
A multidisciplinary team provide liaison geriatric input to frail older adults in TUH. This team carries out comprehensive geriatric assessments (CGAs) on consulted patients or those with frailty attending Emergency Department identified using a Variable Indicative of Placement risk (VIP) tool. Liaison team collated data on frailty scores, falls, diabetes diagnosis, medications and diabetes complications including hypoglycaemia. Results 58 of 213 patients reviewed by the liaison team from Sept to Nov had a diagnosis of type 2 diabetes (27.2%). The median age was 84. The average Clinical Frailty Scale score was 5.7 indicating mild to moderate frailty. 24 (31.5%) of diabetic patients had falls. 21 of these who had falls were prescribed either Sulphonylureas and/or Insulin. 5 patients had a documented history of hypoglycaemia; two of these patients were on insulin, and one was on a Sulphonylurea.

Conclusion:
The management of frail older adults with type 2 diabetes is complicated by multimorbidity and increased risk of adverse effects of treatment including hypoglycaemia. The assessment of frailty may enhance the management of older diabetic patients identifying those at high risk of adverse outcomes.

Michelle Byrne, Department of Pharmacy, University Hospital Limerick

"Paracetamol: From simple analgesic to hepatotoxin. Aim: To identify potential risk factors, pharmacological mechanisms and metabolic pathways associated with the development of liver injury/failure in four inpatients following administration of IV Paracetamol at UHL."

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Objectives:
The intent of this study is to: • Identify risk factors which predisposed four patients to paracetamol toxicity. • Discuss how these risk factors altered the pharmacokinetic metabolism of paracetamol. • Understand how the metabolic pathway associated with paracetamol toxicity allowed for the effective treatment with an antidote.

Method:
This study was a retrospective review of four patients diagnosed with liver injury/failure secondary to IV paracetamol administration between 2016 and 2020 at University Hospital Limerick.

Results:
The following risk factors were identified in the clinical cases as increasing the likelihood of hepatotoxicity following IV paracetamol administration: fasting, malnourishment, low body weight, administration route and overdose (exceeding recommended mg/kg). These risk factors can lead to paracetamol poisoning due to 1) depletion of hepatic glutathione stores (fasting, malnourished) or 2) oversaturation of Phase Two pathways. This alters the metabolism of paracetamol rendering the production of a more toxic metabolite (NAPQI). The treatment of paracetamol induced liver injury can be managed by replenishing glutathione stores with N-Acetylcysteine. (1)(2)

Discussion/Conclusion:
Risk factors that predispose patients to paracetamol toxicity are multifactorial. Therefore a clinical risk assessment should be complete before is commenced on IV paracetamol. Factors to be considered include: malnutrition, fasting state, weight, administration route and hepatic risk factors.

References:
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Aisling O' Connor, University Hospital Limerick, Limerick, Ireland

"Implementation of a Quality Improvement Plan and Monitoring System for a High-Risk Medication at a University Teaching Hospital"

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Background:
Concentrated potassium is a high-risk medication. Incorrect administration can lead to serious adverse effects, including arrhythmia and cardiac arrest. The WHO recommends that healthcare organisations have processes to promote safe practices with this medication (1). The Irish Medication Safety Network (IMSN) has made a series of recommendations regarding concentrated potassium use in hospitals to improve safety. (2) This study will discuss the impact of implementing a Quality Improvement Plan (QIP) to improve compliance with safety procedures for concentrated potassium.

Method:
A baseline audit was completed to assess compliance with standards as outlined in IMSN guidelines. The results of this audit highlighted that the recommended standards were not being met. A QIP was developed and implemented; this included the development of a policy on the management of potassium and the introduction of enhanced safety measures for concentrated potassium. After introducing the QIP, a monthly audit was implemented to measure compliance with these standards.

Results:
Before introducing the QIP, 52% of clinical areas had concentrated potassium stored as recommended; post-QIP, this has increased to 100%. There has been a significant decrease in the number of concentrated potassium vials used monthly in the hospital from 1,200 vials pre-implementation to an average of 600 vials post-implementation. An area for improvement is compliance with the use of potassium registers which is currently around 75%. Conclusion: Implementing a quality improvement plan has seen significant improvements in compliance with some of the recommended safety standards. However, more work is needed to ensure compliance with all standards.

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Aisling O'Reilly, Senior House Officer, Beaumont Hospital Dublin

"This clinical audit was performed in order to document the adherence to the "Management of Adult Asthma in Clinical Practice"(Barry et al 2018) guidelines in terms of appropriate prescription of inhaled corticosteroids in patients with chronic obstructive pulmonary disease and asthma. The goal was to encourage appropriate prescription of inhaled corticosteroids in a population at risk of corticosteroid excess, which in turn carries risk of long term adrenal suppression."

Dr Aisling O'Reilly [1]

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Inhaled corticosteroids (ICS) are not indicated as monotherapy in the long-term management of chronic obstructive pulmonary disease and asthma as per the Medicines Management Programme guidelines- "Management of Adult Asthma in Clinical Practice", Barry et al. 2018 (1). The long-term prescription of ICS alongside long-acting beta agonists (LABAs) is approved for patients with GOLD stage C and D with recurrent exacerbations, despite prior(?) management with LABAs, as per current recommendations (2). Prolonged ICS treatment enhances risk of multiple effects including pneumonia, mycobacterial infections, fragility fractures and progression of diabetes. This audit was performed to rule out non adherence to these recommendations, and bring to attention the appropriate prescribing guidelines for ICS. Secondary outcome was recorded as being the presence of adverse effects due to inhaled corticosteroids as documented in medication records. Data was collected via retrospective medical and medication chart review over a period of 7 days across 6 inpatient wards in a city centre tertiary hospital. Results showed that 11.1% of patients audited remained on inhaled corticosteroid monotherapy. 30% of patients on inhaled corticosteroid therapy (as monotherapy or combination therapy) had documented side effects. Data analysis indicates that despite the presence of prescribing guidelines, there remains patients in the inpatient cohort who are non-cohesive to these recommendations. Concomitantly, adverse effects among patients on ICS mono- or combination therapy remain prevalent. As such, there is margin for increased advocacy of previously published guidelines in the future, with advice on tapering excess dosage of ICS via an awareness campaign.

References:

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Yangyang Wang, Queen's University Belfast

"Higher degree by research and thesis dissecting the mode of action of HDAC6 inhibition in cancer"

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Histone deacetylase 6 (HDAC6) is one of 18 HDAC proteins and uniquely consists of two catalytic domains, locates in the cytoplasm and deacetylates cytoplasmic proteins. Ricolinostat (ACY-1215), a selective HDAC6 inhibitor, is currently undergoing clinical trials in several cancer types, either alone or in combination with existing drugs.

We investigated if HDAC6 inhibition could sensitise Triple Negative Breast Cancer (TNBC) cells to the chemotherapy drug cisplatin. Cal-51 and MDA-MB-231 TNBC cell lines were treated with the pan-HDAC inhibitor SAHA or ACY-1215 and dose response analysis of cisplatin were determined. SAHA and non-selective concentration of ACY-1215 significantly sensitised both cell lines to cisplatin.

While selective HDAC6 inhibition had minimal effects on cisplatin responses in TNBC cells, HDAC6 siRNA reduced the clonogenicity of TNBC cells, which was further reduced in combination with cisplatin. We hypothesize that selective HDAC6 inhibitor effects were reversed by other tubulin deacetylating HDACs such as HDAC8, and Sirt2, or an active CD1 domain that is not targeted with ACY-1215.

To investigate the activity of the HDAC6 CD1 domain a HDAC6 truncated protein consisting of CD1 only and a HDAC6 mutant protein with an inactive CD2 domain was overexpressed in HDAC6 null cells. Western blot analysis showed the deacetylation of alpha-tubulin by the CD1 domain.

In conclusion, loss of HDAC6 expression but not catalytic inhibition potentiated cisplatin responses in TNBC cells in which the lack of CD1 inhibition with ACY-1215 or other cytoplasmic alpha-tubulin deacetylating proteins may explain the poor efficacy of HDAC6 inhibition with ACY-1215.

Fengyu Zhang, Queen's University Belfast

"Investigation of HDAC6 inhibition in Triple Negative Breast Cancer"

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HDAC6 is a unique member of the HDAC protein family because it consists of two catalytic domains and predominantly exists in the cell cytoplasm where it deacetylates cytoplasmic substrates. Despite the potent biochemical effects of HDAC6 inhibitors on tubulin deacetylation, their failure to elicit phenotypic responses indicates a functional tolerance to HDAC6 inhibition in solid tumours.

We hypothesised that the enzymatic independent functions of HDAC6 could be involved in the pathogenesis of solid tumours and investigated the influence of pharmacological inhibition with ACY-1215 and protein knockdown of HDAC6 with siRNA and a HDAC6 targeting PROTAC in TNBC cells. The stable overexpression of wildtype and a catalytically dead HDAC6 mutant in TNBC cells was also investigated. The enzymatic inhibition of HDAC6 was insufficient to inhibit TNBC cell proliferation, while elimination of HDAC6 protein expression led to a significant growth suppression. The overexpression of both full length HDAC6 and the double dead HDAC6 had similar effects on the growth rate of TNBC cells and grew slower than empty vector control cells.

Therefore, the overexpression of HDAC6 in the absence of increased HDAC6 deacetylation contributed to reduced TNBC cell proliferation and suggests that the non-enzymatic function of HDAC6 may play a critical role in TNBC cell proliferation. In conclusion, HDAC6 catalytic domain inhibitors inhibit HDAC6 deacetylation but do not prevent HDAC6 dependent functions in TNBC cells.

Dr Ruadhan O'Laoi, St. James' Hospital

"A retrospective analysis of paracetamol poisonings and n-acetylcysteine administration in a major teaching hospital."

Ruadhan O'Laoi[1]; Cormac Kennedy[1]; Emer Kidney[1]

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Objective: To describe the demographics and relevant clinical indices in patients receiving n-acetylcysteine treatment for paracetamol poisoning.

Background: N-acetylcysteine (NAC) is an effective antidote for paracetamol poisoning, particularly when administered within 8 hours of overdose. In Ireland, the complex '3-bag/21 hour' administration protocol has remained largely unchanged for over 40 years. Modified protocols used in other Western countries, such as the '2-bag/12 hour' SNAP regimen, boast reduced rates of adverse drug reactions and shorter infusion durations without sacrificing efficacy[1,2,3].

Methods: We retrospectively searched all Emergency Department presentations to St James' Hospital in 2019 to identify paracetamol poisonings requiring admission for n-acetylcysteine therapy. We documented demographics, overdose details, rates of adverse drug reactions and relevant clinical time intervals.

Results: 46 presentations were identified. Median age was 27 years old (IQR: 20-39.5 years old) with a female predominance (80%). Median ingested dose of paracetamol was 15g (IQR: 10-24g). 50% of presentations featured a co-ingestant. The median time from overdose to presentation was 2hr 35m (IQR: 1h 20m – 6hr 30) and 7hr 7m (IQR: 5hr 50m – 11hr) to NAC administration. The median delay in switching NAC bags 1-2 was 52m (IQR: 30m – 1hr 30m). The median delay in switching NAC bag 2-3 was 1h 15m (IQR: 35m – 2h 45m). Following NAC, 67% experienced gastrointestinal adverse effects and 2% experienced an anaphylactoid reaction. Median length of stay was 47 hours (IQR: 31- 66hr)

Conclusion: Use of a modified n-acetylcysteine regimen in Ireland could decrease rates of adverse drug reactions, treatment interruption and overall length of stay in patients presenting with paracetamol poisoning.