RCoA Research, Education & Travel Grants 2015

Award: The Ernest Leach Fund

Applicant: Dr John Williams

Project Title: Effect of one-week ingestion of the opioid analgesic codeine on immune function in young healthy male volunteers

Project Description:

1) Today analgesic agents are the most commonly prescribed medications used in primary care within the UK, with prescriptions for opioids increasing by as much as 10% per annum in this setting. Furthermore, the Food and Drug Administration (FDA) in the USA has raised concerns about the possible harmful effects of opioids when used in a chronic fashion. These concerns have encouraged the FDA to demand greater research to be undertaken into the prevalence of and mechanisms underpinning the chronic adverse effects of opioids. Moreover, the aims of this project are in line with those of the NIAA, which aims to improve patient care by translating research findings into clinical practice.

Opioid medications are capable of immune suppression via unknown mechanisms. Years of in vitro experiments have concluded that direct effects on immune cells via classical opioid receptors are unlikely. Opioids have varying effects on the hypothalamic-pituitary-adrenal (HPA) axis in animal and human models. These changes have the potential to cause immunosuppression. Therefore, we wish to study whether one-week ingestion of codeine in healthy volunteers has the potential to cause immunosuppression via changes in the HPA axis.

2) We aim to study 10 healthy male volunteers. The study will be conducted at the University of Nottingham and has received ethical approval. Following informed written consent, participants with attend the first day and a 16G cannula will be inserted into the antecubital fossa and 30 millilitres of blood drawn from this for; FBC, LFT, U&E, baseline plasma cortisol, corticotrophin releasing hormone (CRH), adrenocorticotrophic hormone (ACTH), RNA and inflammatory markers. After this Synacthen will be administered intravenously. 30 minutes after this 20 millilitres of venous blood will be drawn again for cortisol, CRH and ACTH. Participants will then be given the study medication (Codeine 30mg tablets) and a diary in order to monitor compliance. The participants will be asked to consume one tablet of codeine four times per day for the next seven days. The above plasma levels will be repeated after 7 days of Codeine administration to identify any changes. Results will then be analysed with repeated measures t-test or Wilcoxon signed rank test as appropriate.

3) We aim to complete the study within one year. The proposed starting date is October 1st 2015. The funding is required to cover the costs of the study medications, costs associated with RNA extraction equipment as well as costs associated with ELISA analysis. We believe acquiring this funding will be essential in order to undertake this research. The results of which could have important implications in understanding the mechanisms of opioid-induced immunosuppression and therefore have important implications for patient safety.