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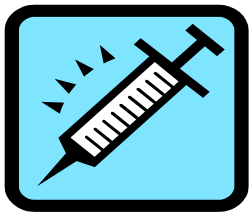
Trimethoprim use in older patients. Use of co-trimoxazole (combination of trimethoprim and sulfamethoxazole) has been associated with adverse outcomes including an increased risk of sudden death (SD). It is not known if these adverse risks are similar for trimethoprim alone, which is used as a first-line option for treatment of uncomplicated urinary tract infections (UTI). A recent study assessed the association between use of trimethoprim and acute kidney injury (AKI), hyperkalaemia (HK) and SD in patients ≥65 years ***(BMJ 2018;360:k341)***. The study period from April 1997 to September 2015 used the UK Clinical Practice Research Datalink which links to hospital records from the Hospital Episode Statistics (HES) database. Patients ≥65 years who were prescribed an antibiotic for a UTI (trimethoprim, amoxicillin, cephalexin, ciprofloxacin or nitrofurantoin) were identified (exclusion criteria included patients with end stage renal disease) and their record was checked for a diagnosis of AKI, HK and SD within 14 days following antibiotic initiation for a UTI. The study adjusted for confounders including chronic co-morbidity, history of renal or urological disease, baseline renal function and use of renin-angiotensin system blockers or potassium sparing diuretics. The study found that **compared to amoxicillin the odds of AKI were significantly higher for trimethoprim (adjusted odds ratios [OR] 1.72) and ciprofloxacin (OR 1.48); the odds of HK occurring were significantly higher only for trimethoprim (OR 2.27)**. The OR for SD was similar for amoxicillin and trimethoprim and the other antibiotics. The authors recommend that for patients at risk of AKI and HK, other antibiotics should be considered apart from trimethoprim, but if this is not possible, monitoring of renal function and potassium should be performed, in line with the prescribing information for trimethoprim. [**Editor's note**: readers are reminded of the HSE Antibiotic Prescribing guidelines available at: ***https://www.hse.ie/eng/services/list/2/gp/antibiotic-prescribing/]***

Do not exceed the recommended dose of paracetamol! Paracetamol, present in many over-the-counter (OTC) and prescription medicines is considered safe to use when dosed as directed (maximum recommended dose in adults is 4g/day), but, in overdose (OD) has been associated with liver injury. While many paracetamol ODs are the result of deliberate self-harm, it is estimated that a substantial proportion are due to unintentional OD. There is a lack of prospective data on patterns of general population self-administration of paracetamol. A US study aimed to estimate the prevalence of excess paracetamol use and associated seasonal variation ***(Br J Clin Pharmacol 2018, DOI:10.1111/bcp.13551)***. The study included US volunteers aged ≥18 years recruited from multiple online research panels (from March 2011 to 2016), who responded to e-mails to participate in a study. Inclusion criteria were those who reported using paracetamol in the previous 30 days. After enrolling in the study, respondents were sent a daily e-mail for 7 days asking them to complete an online diary medication use for the previous 24 hours (patients selected from a comprehensive list of paracetamol-containing medications) and completion of an exit survey at the end of the week. There were 48,803 responders who met the study criteria and 18,689 completed 7 days of diaries and an exit survey. Of those who completed the study, 14,481 reported paracetamol use during the study of which 7991 (52.2%) reported using paracetamol on ≥4 diary days. **A total of 6.3% of users exceeded 4g paracetamol on ≥1 day and 8g paracetamol was exceeded by 1.2% of users on ≥1 day**. Excess paracetamol use was more likely to occur during the cold/flu season than for off-season symptoms; this was primarily due to an increased use of OTC combination medicines designed to treat upper respiratory cold/flu symptoms. The study included individuals who may have been relatively frequent paracetamol users and therefore is likely to over-estimate the overall population rates exceeding 4g and 8g paracetamol / daily. However the authors conclude that the study suggests that there is a **need for public education to discourage paracetamol use that exceeds the recommended maximum dose**.

How to improve medication adherence in cardiovascular disease. Cardiovascular disease (CVD) is the leading cause of death worldwide – estimated at 17.9 million in 2015. At least 75% of those deaths occurred in countries with limited resources and about 30% occurred in patients with prevalent CVD. Statins, aspirin and anti-hypertensive medicines can substantially reduce CVD mortality and morbidity in those with existing atherosclerotic (AS) CVD. However non-adherence to these medicines (defined as taking <80% of prescribed doses) is an ongoing problem. Reasons for non-adherence to ASCVD medicines include costs, misunderstandings about risks and benefits, adverse drug reactions and lack of availability. **A recent systematic review evaluated and compared the effects of strategies to improve adherence to medicines used for the secondary prevention of ASCVD**. A total of 17 randomised controlled trials (RCTs; n=17,448 patients) were included in the review (***Heart 2018; doi.10.1136/heartjnl-2017-312571***). These RCTs had used various types of intervention(s) to improve adherence, which was assessed either through self-report, pharmacy data, pill count or electronic pill bottle opening, compared with routine care (control). The primary outcome was adherence to the ASCVD medicines; secondary outcomes included blood pressure (BP) control and rates of acute coronary syndrome, myocardial infarction (MI), stroke and percutaneous coronary intervention. **Results:** Twelve of the 17 RCTs showed a statistically significant benefit on adherence for the active intervention(s) versus the controls (overall adherence rates of 44 to 99% versus 13 to 96% respectively). Of interest, 3 interventions (from 3 separate RCTs) demonstrated a significant improvement in both adherence and clinical parameters (BP reduction). The interventions were: (1) **the use of a short message service (SMS) reminder** before every intake of CVD medication for 8 weeks following discharge post-MI (2) **involvement of a community health worker in promoting adherence** and (3) **use of a fixed-dose combination medication**. The review did not find evidence that ASCVD clinical outcomes were improved overall; however this was thought to be due to the fact that the studies were not powered for these outcomes and also because of the short-term nature of many of the studies. The review was limited by the lack of uniformity between the RCTs in intervention type and in measuring adherence which precluded a meta-analysis. However, the authors note that as the number of individuals with ASCVD rises globally, non-adherence will be a large source of poor health. **The findings from this review identified simple low-cost-interventions with potential for scaling in a low-resource setting, which resulted in increased adherence**. The authors conclude that well-powered longer-term trials are needed to determine whether these short-term changes in adherence can be maintained and lead to differences in clinical events in the long-term.



Measles outbreak in Europe. Measles is a highly infectious disease, which is most common in young children, however it can affect anyone at any age. There has been an increase in the number of cases of measles reported in Ireland for the first quarter of 2018, compared to 2017 ***(www.hpsc.ie/notifiablediseases/weeklyidreports/ID%20Week%2012.pdf).*** There are also several ongoing measles outbreaks in Europe. Since January 2018, the highest numbers of measles cases in the EU were Greece (1,008), Romania (757), France (429) and Italy (164) ***(www.hse.ie)***. **Vaccination with measles, mumps, rubella (MMR) vaccine is the only way to protect against measles;** two doses of MMR vaccine are required to give the best protection. In addition to children who have not been age-appropriately vaccinated, adults could also be at risk of measles if they are <40 years of age and have never had measles or did not have 2 doses of a measles vaccine. The Health Service Executive (HSE) recommends that **individuals travelling to Europe and other parts of the world where measles outbreaks are occurring should ensure that they have had the MMR vaccine**. Full recommendations for MMR vaccination are available in the immunisation guidelines https://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. References are available on request. This ***newsletter is produced by the National Medicines Information Centre, St. James's Hospital (SJH) Dublin 8 and Dept of Therapeutics Trinity College, Trinity Centre, SJH.*** *Tel: Direct Line (01) 473 0589 or 1850 727 727 Email: nmic@stjames.ie*