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Identifying "at-risk" NSAID users. Non-steroidal anti-inflammatory drugs (NSAIDs) are amongst the most frequently prescribed drugs, and are associated with adverse effects including gastrointestinal (GI) toxicity. The prevalence of GI complaints varies between 5-50% of patients receiving traditional and cyclooxygenase-2 selective NSAIDs. Co-prescription of a gastroprotective agent (such as a proton pump inhibitor) is frequently given to minimise GI risk associated with NSAID use; however this strategy is only cost-effective in NSAID users at high GI risk. A recent review of guidelines and consensus agreements (*Drug Saf 2010;33(6): 443-453*) sought to identify and stratify risk factors for GI complaints in NSAID users, and to evaluate the contribution of over the counter (OTC) NSAIDs. The "definite" risk factors, present in all analysed guidelines (n=9) were: **history of complicated (peptic ulcer bleeding, obstruction or perforation) and uncomplicated peptic ulcer disease, older age (ranging from 60-75 years), concomitant anticoagulant use, concomitant corticosteroid use and low-dose aspirin or multiple NSAID use.** Risk factors were defined as "controversial" if they were not described in all the guidelines; these included a history of GI symptoms, high-dose NSAID use, concomitant clopidogrel therapy, concomitant selective serotonin reuptake inhibitor (SSRI) use and co-morbidity (e.g. rheumatoid arthritis and cardiovascular disease). Infection with *Helicobacter pylori* was defined as an additive risk factor for GI events in NSAID users. Although the use of OTC NSAIDs (which could contribute to the incidence of GI events) has been increasing, the review found little information on their use in the guidelines and no information regarding the identification of OTC NSAID users as being at risk of GI events. The authors conclude that while the definite risk factors were undisputed in all reviewed guidelines, **further research is required in relation to the "controversial" risk factors (including concomitant clopidogrel and SSRI use).** The possibility of OTC use should also be considered in the identification of patients at risk of a GI event.



Does a spoonful of sugar really help the medicine go down? Current evidence suggests that administration of oral sweet solutions (usually sucrose or glucose) are effective analgesics in neonates for minor painful procedures; however there is conflicting evidence as to whether they are effective in older infants. A recent review sought to ascertain the **effectiveness of the administration of sweet solutions during painful procedures for infants beyond the neonatal period up to 12 months** (*Arch Dis Child 2010.doi:10.1136adc.2009.174227*). The review included randomised controlled trials (RCTs) (n=14) where infants beyond the neonatal period up to 12 months of age were administered either sucrose / glucose of various concentrations versus water or placebo during immunisation. The systematic review found that **oral administration of either sucrose or glucose resulted in reduced crying incidence, crying duration and composite pain scores compared to placebo/no treatment in 13 of the 14 studies.** Meta-analyses were performed for 3 outcomes: proportion of crying times post immunisation, incidence of cry and duration of cry until crying cessation. Results showed a 10% mean reduction in proportion of crying time, and a 20% reduction in relative risk (RR) for crying incidence for infants administered sweet solutions compared to placebo. A clinically small reduction of -12 seconds in crying duration was also noted in the sweet solution-treated subjects (but 2 heterogeneous RCTs were omitted from this analysis). Due to inconsistencies in the volumes and concentrations of the sweet solutions used in the studies an optimal dose could not be determined, however results suggested that higher concentrations than those used for neonates may be more effective. The authors recommend that the administration of sucrose or glucose along with other recommended physical or psychological pain reduction strategies should be considered when immunising infants and that further research is required on the optimum concentration and dose regimen.



Incidence of imported malaria in Ireland. Malaria is a risk to anyone travelling to an endemic country, however deaths from malaria are largely preventable. The May edition of Epi-Insight contains the malaria figures for 2009: 90 cases of malaria were notified in Ireland (including one death), which was similar to numbers reported for the previous three years (www.hpsc.ie). The primary reason for travel in those diagnosed with malaria was reported as "visiting family in country of origin". Where country of infection was reported (n=62 cases), over half were exposed in Nigeria; the remainder were from other Sub-Saharan African or Asian countries. *Plasmodium falciparum* was

responsible for the majority of cases acquired in Africa while *P. vivax* was most common from Asia. **Half of all the cases of malaria in Ireland in 2009 were notified during the 3rd quarter**, which coincides with the summer holiday period. The peak at this time was most prominent in those who reported their reason for travel as "visiting family in country of origin", while cases amongst those who reported reason for travel as "holidaymakers" were more common during the winter months. The report suggests that strong promotion of prevention of malaria in the immigrant sub-group who are visiting family may have the greatest impact in reducing malaria. Preventive measures include: sleeping under insecticide-treated bed nets, indoor spraying in endemic areas with appropriate insecticides, prevention of malaria in pregnant women, prompt diagnosis and treatment with effective drugs. [Editor's note: Useful fact sheets are available for travellers on preventing malaria: they can be downloaded from the HPSC website: www.hpsc.ie]



Time to treatment vs. outcome in ischaemic stroke. Many large randomised controlled trials (RCTs) have shown that early administration of intravenous recombinant tissue plasminogen activator (rt-PA) after ischaemic stroke improves outcomes. However, stroke registries have confirmed that some patients are treated with rt-PA beyond the currently approved time of 3 hours from stroke onset. A pooled analysis of eight RCTs was published recently which re-examined the effect of time to treatment with intravenous rt-PA (alteplase) on therapeutic benefit vs. clinical risk (*Lancet 2010;375:1695-703*). Inclusion criteria included a clinical diagnosis of a clearly defined time of stroke onset and a CT scan excluding

intracranial haemorrhage. Statistical analyses were used to assess the relation between stroke onset to start of treatment (OST) on favourable 3-month outcome, mortality, and occurrence of clinically relevant parenchymal haemorrhage. A total of 3,670 patients (1,850 allocated to alteplase and 1,820 to placebo), whose treatment was started within 360 min of stroke onset, were included in the analysis. The results found that the odds of a favourable 3-month outcome increased as the OST decreased (p=0.0269); **there was no benefit of alteplase treatment seen after 270 minutes**. The adjusted odds of a favourable 3-month outcome were: 2.55 from 0-90 min, 1.64 from 91-180 min, 1.34 from 181-270 min, and 1.22 from 271-360 min in the alteplase vs. placebo groups. **The adjusted odds for mortality increased with OST** ranging from 0.78 from 0-90 min, to 1.49 from 271-360 min. Large parenchymal haemorrhages were seen in 5.2% of patients assigned to alteplase and 1% to placebo; no relationship to OST was noted. The authors conclude their analysis shows that treatment with thrombolysis up to 4.5 hours after stroke onset enhances the chance of a favourable outcome, however the greatest benefit comes from earlier treatment and that mortality increases with OST longer than 4.5 hours. An accompanying editorial (*Lancet 2010; 373:1667-1668*) advises that the study adds to the evidence that the benefits of thrombolysis decrease substantially over time. An important new finding was that later onset (>4.5 hours) to start of treatment was associated with increased mortality. It concludes that these findings mandate a renewed commitment by clinicians and policy makers to foster very early intervention which includes increasing the proportion of possible stroke patients arriving to designated stroke centres in the first hour after ischaemia.