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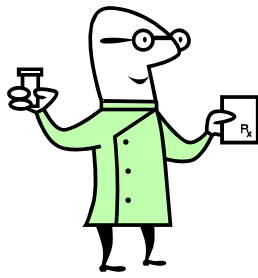
Potential Interaction between Clopidogrel and PPIs. As highlighted in last month's TT newsletter, several recently published studies have suggested that a significant interaction might occur between clopidogrel and proton pump inhibitors (PPIs), making clopidogrel less effective, and resulting in patients being at increased risk of thrombotic events. The Irish Medicines Board (IMB) and the European Medicines Agency (EMA) have issued public statements on this issue, following joint review of all currently available scientific data by the EU regulatory authorities. The IMB and EMA now recommend that:

Concomitant use of PPIs and clopidogrel should be discouraged unless absolutely necessary

The prescribing information of all clopidogrel-containing medicines will be amended in the near future to include this recommendation. The EMA also recommends that further information is needed in relation to the mechanism of inhibition of clopidogrel metabolism by other medicines and to assess the implications of possible genetic variations in the activation of clopidogrel (see May TT newsletter for more details on this). Further background information is available at: www.imb.ie; and <http://www.emea.europa.eu/humandocs/PDFs/EPAR/Plavix/32895609en.pdf>



Intensive glucose control of diabetic patients. Type 2 diabetes mellitus (DM) is a well-established risk factor for cardiovascular disease (CVD). Evidence has shown that intensive control of glucose in patients with type 2 diabetes mellitus (DM) has substantial benefits on microvascular outcomes, however individual randomised controlled trials (RCTs) have not shown similar consistent benefits on macrovascular outcomes. A recently published meta-analysis evaluated whether intensive lowering of glucose in patients with type 2 DM might reduce macrovascular events and all cause mortality (*Lancet* 2009;373:1765-72). The analysis included 5 RCTs involving 33,040 type 2 DM patients, who had been randomly assigned to receive either intensive lowering of glucose versus a standard regimen (placebo, standard care or glycaemic control of reduced intensity). Each trial had evaluated CVD outcomes as the primary endpoint. Participants were enrolled from predominantly western populations: 1 study enrolled individuals within 1 year after diagnosis, the remaining 4 studies enrolled participants with longstanding DM. The meta-analysis found that the mean HbA1c was 0.9% lower for those patients with intensive glucose-lowering treatment versus the standard regimen. **Patients with intensive glucose-lowering treatment had significantly reduced non-fatal myocardial infarction** (17% reduction - OR 0.83, 95% CI 0.75-0.93) **and coronary heart disease (CHD)** (15% reduction - OR 0.85, 0.77-0.93). Intensive glucose-lowering treatment did not significantly affect the incidence of stroke (OR 0.93, 0.81-1.06) or all cause mortality (OR 1.02, 0.87-1.19). As expected, patients on intensive glucose-lowering treatment had more hypoglycaemic events than those on standard therapy (38% vs. 28.6%) and also weighed more than those on standard treatment at the end of the study. There was no significant statistical heterogeneity across the studies with respect to the effects of the different glucose lowering regimens on non-fatal MI, CHD or stroke, although significant heterogeneity was noted with respect to all cause mortality. A limitation was that since this was a meta-analysis, individual studies varied with respect to patient demographics, duration of follow-up and the drugs used for intensive glucose control. However, the authors conclude that the study findings provide reassurance about the effectiveness of tight glycaemic control for CVD risk reduction, without increasing the risk of death.



"Why look at an SPC?" The background to the Summary of Product Characteristics (SmPC/ SPC) was recently reviewed (*DTB 2009; 47: 56-58*). The SmPC is the legal document providing approved prescribing information (including licensed indications, precautions for use and safety and efficacy data) on a medicinal product (MP). The format of the SmPC is standardised throughout the EU. The original draft is generated by the company that holds the licence (the "Marketing Authorisation Holder"), based on data generated during the development of that MP; however the final wording must be agreed with the

regulatory authority (the EMEA/IMB) and cannot be changed subsequently without formal regulatory approval. The text of the SmPC is reviewed regularly and is updated to include any new safety data or new indications for use, once the MP is on the market. The SmPCs for authorised MPs in Ireland are available on www.imb.ie (under human medicines listing) and at www.medicines.ie, the IPHA website, which has recently been updated to facilitate searching under either the non-proprietary or brand name of a MP.



Updated "WHO guidelines on Hand Hygiene in Healthcare" now available.

Healthcare-associated infection (HCAI) is a major problem for patient safety. Estimates suggest that >1.4 million patients worldwide are affected at any one time. The WHO recently undertook an extensive systematic review of all evidence related to hand hygiene in healthcare workers (HCWs) and the recommendations in the new guideline are relevant for all aspects of healthcare. **Transmission of HCAI**

pathogens requires 5 sequential steps: (i) presence of organisms on patient's skin or inanimate objects immediately surrounding the patient; (ii) transfer of the pathogens onto the HCW's hands; (iii) organisms to be capable of surviving for at least several minutes on the HCW's hands; (iv) HCW hand hygiene inadequate or omitted entirely; (v) the contaminated hand(s) of the HCW to come into direct contact with another patients / object which will come into direct contact with the patient. It is difficult to compare the **relative efficacy** of the various methods available for hand hygiene, using the available data. However the report notes that antiseptic detergents (such as chlorhexidine, iodine, hexachlorophene) are usually more efficacious than plain soap and that alcohol-based rubs (which generally contain ethanol, isopropanol, n-propanol) are more efficacious than antiseptic detergents.

The WHO guideline includes the following recommendations: hand hygiene is needed before and after touching a patient; before touching an invasive device used for patient care, whether or not gloves are used; after contact with body fluids or excretions, mucous membranes, non-intact skin or wound dressing; if moving from a contaminated body site to another body site on the same patient; after touching inanimate surfaces and objects in the immediate vicinity; and after removing gloves. Hand hygiene is also needed before handling medication or preparing food for a patient. **Glove use does not replace the need for hand hygiene.** Hands should be washed with soap and water when visibly dirty, when soiled with blood or other body fluids or after using the toilet; hand washing is also preferred when exposure to potential spore-forming pathogens such as *Clostridium difficile*, is strongly suspected or proven. In all other clinical situations, use an alcohol-based hand rub (if available) as the preferred means for routine hand antisepsis. **Soap and alcohol-based hand rub should not be used together.** The report notes that care should be taken when choosing a product for cleaning hands to ensure there is no interaction between it and gloves or other skin care products used in the healthcare location. HCWs should be educated in appropriate hand-care practices in order to reduce the risk of irritant contact dermatitis and other skin damage (a change in hand rub products may be needed). The WHO report provides easy-to-follow guidance on the correct hand hygiene technique depending on whether the alcohol-based hand rub or hand washing is to be used. [A summary of the WHO recommendations is available at www.medscape.com/viewarticle/702406 and the full scientific report is available at: www.whqlibdoc.who.int/publications/2009/9789241597906_eng.pdf]