Therapeutics Today

June *2005*
Number 6

Holidays on the Run! Traveller's diarrhoea (TD), defined as the passage of ≥3 unformed stools over 24 hours was reviewed recently ***(Lancet Infect Dis 2005; 5: 349-60).*** Symptoms start during or shortly after a period of foreign travel; diarrhoea is often accompanied by other clinical features such as nausea, vomiting, abdominal pain, fever, faecal urgency, tenesmus and blood/mucus in the stools. TD is estimated to have an attack rate of 20-50% and is on the increase due to increased overseas travel; travellers from high-income countries have the **highest attack rates**. Destination is the most powerful predictor of TD; the highest risks (20-60%) are recorded for the Middle East, South/Southeast Asia, South/Central America and low-income African countries. Travellers on self-arranged itineraries (trekkers, campers) have increased risk, probably reflecting the hygiene standards of facilities they use. **The causal pathogen** is identifiable in 40-60% of TD, of which 85% are bacteria. Worldwide, enterotoxigenic *E coli* (ETEC) are the commonest bacterial pathogens isolated. *Campylobacter jejuni*, salmonellae and shigellae also account for many cases, depending on the region. Bacterial infection may result in a toxin-mediated illness (e.g. short-lived diarrhoea) or an invasive infection, which may be more chronic and associated with systemic symptoms (e.g. fever); frequently there is overlap between the 2 types. Viruses account for a minority of illnesses.

Treatment: The main objectives include prevention of dehydration, reduction of symptoms and duration of TD. All TD sufferers should ensure adequate intake of fluids during an episode. **Increasing standard fluids (e.g. soft drinks with added salt) may be adequate for adults. Oral rehydration therapy is recommended for infants, young children, the elderly and severe TD cases.** Young infants should receive breast milk or lactose-free formula. TD sufferers on diuretics or antihypertensive agents may need to reduce or stop these medications temporarily. Loperamide is the anti-motility drug of choice. However, it should not be used in children < 2 years and should be used with caution in the presence of invasive bacterial TD as it may worsen the condition. Many TD episodes will resolve with rehydration +/- loperamide.

Anti-microbial agents +/- loperamide are effective in reducing the duration and severity of symptoms of TD. Fluoroquinolones are effective (e.g. ciprofloxacin 750mg given as a single dose* or 500mg BD X 3days). Azithromycin (1g single dose* or 500mg/day X 3days) may also be used. However, overuse may result in development of resistance (which has occurred with co-trimoxazole). Management of chronic TD (i.e. still present on return from holidays) may require advice from microbiology specialist units. [Editor's note: The WHO has a useful website on international travel and health. www.who.int/ith/index.html] *single dose regimen not included in SPC.

Hair to dye for…. Recent observational studies have suggested that the use of hair dyes may act as a risk factor for several types of cancer. A systematic evaluation of these studies was recently published ***(JAMA 2005; 293: 2516-25).*** A total of 79 studies were reviewed, including 40 in haematopoietic cancers, 14 in breast cancer and 10 in bladder cancer; these included both male and female personal users of permanent dyes with varying levels of exposures. Results showed no strong evidence of a marked increased risk of cancer among hair dye users. Of interest there was a slightly increased risk (15%) in haematopoietic cancers that related specifically to data on use in men. However, there was significant heterogeneity in these data, which calls into question the relevance of this finding. The authors state that the results support the view that there are no grounds for public health concern. They recommend that further studies should be undertaken in the occupational setting (e.g. hairdressing salons) where exposure to hair dyes is more prolonged and at higher concentration compared with personal use.

Air travel and the risk of DVT. In recent years, there have been several reports on the risk of developing deep venous thrombosis (DVT) +/- pulmonary embolism (PE) with air travel. The British Committee for Standards in Haematology (BCSH) recently issued an interim guideline on this topic (***www.bcshguidelines.com*)**. Currently available data suggest that the risk of a fatal DVT after a trans-atlantic air flight is less than one in a million; the risk is related to the duration of travel (lowest risk for journeys of < 6 hours) and the presence of additional risk factors, e.g. surgery in the previous few weeks. The guideline outlines recommendations for flights > 6 hours based on low, moderate or high risk as follows:

Low risk (no history of DVT/PE; no surgery in the previous 4 weeks): Recommendations are to a) regularly flex ankles to contract calf muscles during the flight, b) not to take sleeping tablets and c) not to drink excessive amounts of alcohol. **Moderate risk** (history of DVT; surgery with general anaesthetic > 30 minutes 4-8 weeks previously): Recommendations as for low risk group PLUS use of compression travel socks*. **High risk** (surgery within previous 4 weeks): Recommendations as for moderate risk group PLUS consideration of single injection of low molecular weight heparin (LMWH) before departure. **Groups for Special consideration**: patients with a positive history of DVT/PE and additional risk factors for recurrence (e.g. cancer) may need LMWH at the discretion of their own physician. Those with plaster casts should be considered for a split cast to reduce the risk of compression. Patients on anticoagulant treatment are at low risk of DVT but if flying within 2 weeks of new DVT/PE, expert advice should be sought. Finally, the **guideline states that there is no evidence to support the use of aspirin in any category.** The WHO is currently researching this area ***(www.who.int/cardiovascular_diseases/wright_project/en)*** and the results will be published next year. [*should be properly fitted, below-knee socks which provide 15-30mmHg compression at the ankle] ***(Chest 2004; 126: 338S-400S)***

Cost effective prescribing of the proton pump inhibitors. It is estimated that 10% of the Irish population seek their GP's advice for dyspeptic symptoms each year. Total expenditure under the community drugs schemes in Ireland on the proton pump inhibitors (PPIs) for patients with dyspepsia was approximately €73 million in 2003, an 8-fold increase since 1995. **The PPIs**, which include omeprazole (e.g. Losec MUPS®), lansoprazole (Zoton®), pantoprazole (Protium®), rabeprazole (Pariet®) and esomeprazole (Nexium®), **are the most expensive drug group reimbursed under the community drugs schemes, accounting for over 10% of total drug expenditure**. The National Centre for Pharmacoeconomics (NCPE) recently studied current Irish prescribing trends for PPIs to see if cost savings might be made by changes in prescribing practice ***(IMJ 2005; 98 (3): 78-80)***. The GMS prescribing database and current clinical and cost effectiveness guidelines issued by NICE (UK National Institute for Health and Clinical Excellence) on the use of PPIs in the treatment of dyspepsia ***(www.nice.org.uk)*** were used in the evaluation. A detailed analysis of PPI prescribing was undertaken over a 12-month period (Nov 2002-Oct 2003). As maintenance therapy with PPIs accounts for the majority of expenditure (> 80% of costs associated with omeprazole under the GMS scheme during the study period) data from all patients who received uninterrupted PPI therapy for at least 3 months were included in the study. The dose of each PPI used for maintenance therapy was also determined. Results showed that the majority of patients were prescribed a higher (i.e. healing) dose, although NICE recommends use of the lowest effective dose for maintenance, once symptoms have come under control. Substitution, in accordance with therapeutic indication, of the PPI with the greatest individual cost i.e. Losec MUPS® with any of the alternative PPIs listed above or any generic omeprazole was estimated to result in savings. Estimated cost savings of >€6 million per year were presented when Losec MUPS® was substituted with the following: the generic omeprazole preparations Ulcid®, Lopraz® or rabeprazole (Pariet®) or pantoprazole (Protium®). Savings could be further enhanced by reducing the dose of PPIs to the lowest effective dose for maintenance therapy.

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 and the Trinity College Department of Therapeutics, Trinity Centre, St. James's Hospital, Dublin 8. Tel:Direct Line (01) 473 0589 or 1850 727 727 Fax: (01) 473 0596 Email: nmic@stjames.ie*