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Safety Update for Champix®. The European Medicines Agency (EMA) recently issued a safety warning about the use of Champix® (varenicline) authorised for smoking cessation in adults. Reports of "suicidal ideation" and suicide attempts in people taking varenicline have been received; however, it is difficult to know whether this is due to varenicline, as stopping smoking itself may be associated with depression particularly in people with mental health problems. **The EMA has recommended that the product information should be updated to warn doctors that depression (including suicidal ideation and suicide attempts) have been reported in patients on varenicline for smoking cessation.** The EMA also advises that patients taking varenicline who develop suicidal thoughts should stop their treatment and contact their doctor immediately. [Editor's note: Further information, including a Q & A document is available on the EMA and IMB websites (www.imb.ie; www.ema.europa.eu)].



Continued use of anti-ulcer therapy may be inappropriate after hospital discharge. Critically ill patients may suffer from acute gastrointestinal (GI) bleeding, due to stress-induced GI ulceration. The efficacy of gastric acid suppressants (GAS) in reducing the incidence of clinically significant stress-induced GI bleeding has been proven in multiple studies and most hospital intensive care units (ICUs) now have guidelines for initiation of stress ulcer prophylactic therapy (such as H2 antagonists; proton pump inhibitors) for at-risk patients. However, the majority of these patients do not need such therapy after discharge from ICU / hospital. A recent study reviewed the use of GAS in ICU patients in a tertiary referral hospital during a 3-month period (*Ann Pharmacother* 2007; 41: 1611-6). Of 394 eligible patients (n=257 surgical; 137 medical), 357 were prescribed GAS and 223 of these were eventually discharged home on the medication. Results showed that 127 had a clear indication for continued use of such medications (including diagnosis of gastro-oesophageal reflux or peptic ulceration, GI bleed during hospitalisation or in the previous year prior to admission, chronic ventilation or prescriber-recorded reason for continuing such therapy). **However, 96 (24% of the original study cohort) had no clear documented indication for continued use of GAS.** The follow-up notes were sparse with respect to continuing medication, but only 1/55 patients for whom data were available had been instructed to discontinue the medication after approximately 170 days of therapy; the authors estimated that the cost of omeprazole 40mg daily in one patient for around that period of time was \$1453 (approximately €1000). In addition, chronic use of GAS may be associated with adverse drug reactions and drug interactions. The authors conclude that more education is needed for prescribers about appropriate use and discontinuation of GAS in these patients; they also recommend that greater vigilance should be exercised in the assessment of appropriate use of medications at all points of care (hospital admission, transfer, discharge to primary care) in critically ill patients.



Medicines for Children. Recent studies have shown widespread use of unauthorised and "off-label" drugs to treat children in hospital and the community; approximately 2/3 of children treated in hospital receive at least one unauthorised / off-label drug. The use of such medicines in children is more likely to be associated with drug toxicity. Europe recently introduced legislation to ensure that drugs used for children are appropriately investigated and authorised (*BMJ* 2007; 335: 1221-3). Drug companies will be obliged to develop and agree a "paediatric investigational plan" with the EMA for each new drug. Drug development for children is more expensive than for adults since they need tailored formulations (e.g. suspensions for younger children). Therefore, the EU legislation provides financial incentives (6 months' additional marketing exclusivity) for the drug industry to study drugs in children. Older medicines can also be developed for children; if successful, the company will be granted 10 years of patent protection. This new legislative initiative should help prescribers in the management of their younger patients. Read all about this initiative and the expert scientific committee that will oversee the process at www.ema.europa.eu.



Acute bronchiolitis. Acute bronchiolitis (AB) is a major cause of morbidity in infants. Its management was recently reviewed (*BMJ 2007; 335: 1037-1041*). AB is a viral illness (occurring Nov-March) characterised by fever, nasal discharge and a dry, wheezy cough. Eighty percent of cases are caused by Respiratory Syncytial Virus (RSV); other causative agents include: rhinovirus, human metapneumovirus, adenovirus, influenza, parainfluenza and enteroviruses. AB mainly affects children <1 year, the majority of whom can be managed in primary care, however 2-3% require hospitalisation. Pre-existing anatomical and/or immunological abnormalities (including maternal smoking in pregnancy) result in RSV presenting as severe bronchiolitis rather than a mild respiratory illness.

Classically, the **clinical presentation of AB** is increasing respiratory distress in a 2-6 month old infant, preceded by a 2-3 day history of coryzal symptoms. The infant will be tachypnoic, have fine inspiratory crackles +/- wheeze and be febrile (not usually $\geq 40^{\circ}\text{C}$). Cyanosis may occur in severe cases; apnoeic episodes may occur particularly in pre-term young infants. The infant is rarely systemically toxic, therefore a toxic child should prompt a search for another diagnosis.

Treatment for AB is primarily supportive; in primary care the main decision is whether the patient requires to be hospitalised. **Absolute indications for hospital admission** include cyanosis or severe respiratory distress, marked lethargy leading to poor feeding, respiratory distress preventing feeding, apnoeic episodes and diagnostic uncertainty. A lower threshold should be used in very young infants, and infants with an important co-morbidity including congenital heart disease, extreme prematurity, Down syndrome or negative social factors.

Investigations: Chest x-ray is not considered useful in typical AB. Investigations in hospital include pulse oximetry and blood gases (to evaluate the need for respiratory support). Blood and urine cultures are taken if the patient is toxic or has a high fever ($\geq 40^{\circ}\text{C}$). The diagnosis of RSV may be confirmed by a nasopharyngeal aspirate and viral immunofluorescence or polymerase chain reaction (PCR). Treatment in hospital typically is supportive (oxygen, tube feeding and IV fluids as required).

Pharmacotherapy: Evidence does not support treatment with antibiotics in uncomplicated AB. Bronchodilators may produce short-term improvement but do not affect clinical outcomes such as reduced ventilation or hospital stay. Similarly there is **no evidence to show any benefit for inhaled or systemic corticosteroids, ribavirin, or RSV immunoglobulin in AB**. Many infants who are hospitalised with AB will have cough and wheeze for several weeks after the episode of AB (post-bronchiolitis syndrome). Most children eventually recover but symptoms may continue intermittently for several years particularly with subsequent viral infections, making their treatment difficult.

Prevention: Breast-feeding may be partially protective and parental smoking should be discouraged. Hygiene promotion in nursery and day-care facilities may decrease community spread. The monoclonal RSV immunoglobulin palivizumab may be given to high-risk infants; this requires monthly injections and offers partial protection. There is no vaccine available for AB and even natural infection does not produce immunity. The relationship between RSV infection and subsequent asthma is controversial. Current evidence suggests that RSV does not "cause" asthma but that pre-existing atopy may be a risk factor for more severe AB.



Is a cuppa good for your bones? A recent study looked at the effects of tea consumption on the skeleton of 1,500 women aged 70-85 years (*Am J Clin Nutr 2007; 86: 1243-7*). Results showed that total hip bone mineral density (BMD) was 2.8% greater in tea drinkers (=83% of group) than in non-tea drinkers; a prospective analysis (n=164) showed that tea drinkers lost an average of 1.6% of their total hip BMD compared with 4% loss in non-tea drinkers during 5 years' follow-up. Results were not affected by whether milk was added to the tea consumed. The authors note that tea is a major dietary source of flavonoids and lignans, some of which have oestrogen-like activities. However, strong tea (with higher caffeine) may not have the same benefit. [Editor's note: although the results suggest that tea consumption has beneficial effects on the skeleton, perhaps we should have a cuppa while awaiting further confirmatory studies!].

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 Fax: (01) 473 0596 Email: nmic@stjames.ie