



# Therapeutics Today

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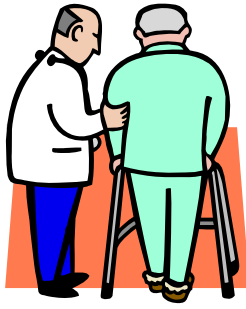


**Tummy trouble!** Functional dyspepsia accounts for up to 5% of visits in primary care. A recent paper reviewed its current management (*JAMA 2008; 299: 555-565*). Functional dyspepsia (FD) may be defined as: any symptom of the upper GI tract (e.g. recurrent pain, heartburn or acid regurgitation, +/- bloating, nausea or vomiting) with no evidence of organic disease to explain the symptoms and/or no evidence that the dyspepsia is due to irritable bowel syndrome. Symptoms should be present for at least 12 weeks within the previous 6-12 months. Although FD is not life-threatening, it can dramatically reduce the patients' quality of life and ability to work. The underlying pathophysiology is unclear but **specialised testing has identified disturbances in GI motor function and altered visceral sensation / hypersensitivity**. However, the cause of these disturbances is unknown and their severity does not accurately predict symptom expression or response to therapy.

**Differential diagnoses** include gastro-oesophageal reflux disease (GORD), peptic ulcer, gastritis, gastroparesis, gall bladder disease, drug-induced, (e.g. NSAIDs) or upper GI malignancy. Physical examination is not helpful in FD but the presence of "alarm symptoms" (including dysphagia, recurrent vomiting, unexplained weight loss, GI bleeding) will identify patients who require urgent attention. **Management:** if the history, examination and initial laboratory tests (routine haematology / biochemistry) do not lead to a diagnosis, the American Gastroenterological Association recommends the following: "test-and-treat" for *H pylori*, prompt endoscopy and empirical anti-secretory therapy. ***H pylori* testing** is recommended only in areas where the community prevalence of infection is greater than 10%, with prompt treatment if positive. **Proton pump inhibitor therapy** is the treatment of choice in FD without *H pylori* infection or in those who fail to respond to *H pylori* eradication. Intermittent treatment may control FD in the longterm. Prokinetic agents (such as **metoclopramide and domperidone**) have been used because many FD sufferers have symptoms of delayed gastric emptying, but the evidence base is poor. **Endoscopy** is usually reserved for patients with onset of symptoms at >55 years, those with alarm symptoms or those who fail other therapies; an organic cause may be found in up to 60% of cases. **Other therapies** such as low dose tricyclic antidepressants or anxiolytic agents have been used but are not authorised for such use. Cognitive behavioural therapy is useful in individual patients. Dietary restrictions are of no benefit except where specific foods are known to trigger an attack. The authors conclude there is no all-encompassing evidence-based therapeutic strategy for managing FD, possibly because of the heterogeneous nature of the symptoms, therefore once organic disease has been ruled out, each patient should be managed on an individual basis. [Editor's note: The BMJ has recently published a study which has shown that "test and treat" and acid suppression are equally cost effective in the initial management of dyspepsia in a UK community care setting. The full article is available online at ([doi:10.1136/bmj.39479.640486.AE](https://doi.org/10.1136/bmj.39479.640486.AE))]



**Soccer may be bad for you!** It is suggested that environmental stress increases the risk of cardiovascular (CVS) events, however, the association between soccer matches and CVS illness or death remains controversial. A recent study evaluated the effect of soccer-related stress on the rate of cardiac emergencies in Germany, a country where soccer is particularly popular (*NEJM 2008; 358: 475-83*). Acute CVS events occurring in German residents in a defined area, during the month of the world cup soccer matches in 2006 were compared with CVS events occurring during several control periods (i.e. no soccer matches). Results showed an event rate of 43.1/day (n=302) during the 7 days when the national team was playing compared with 14.6/day (n=3541) during 242 "control" days. The rate for the 24 days when non-German world cup matches were played was 18.2/day (n=436). The proportion of males affected was higher during the national matches (71%) compared with control days (56.7%) and 47% had pre-existing coronary artery disease, compared with 29.1% of control cases. **Overall the incidence of CVS events was 2.66 times greater during the 7 days of national matches compared with control periods.** The authors conclude that watching a stressful soccer match can double the risk of CVS events and patients with existing CVS disease may need preventive measures. [Editor's note: Perhaps it is just as well that Ireland didn't qualify for the world cup, this time round!]



**New guidance on management of OA** Osteoarthritis (OA) is the commonest form of arthritis and one of the leading causes of pain and disability worldwide. The National Institute for Health and Clinical Excellence (NICE) recently issued guidance on the care and management of OA in adults (*BMJ 2008; 336: 502-3*). OA refers to a clinical syndrome of joint pain accompanied by varying degrees of functional limitation and reduced quality of life (QoL). Knees, hips and small hand joints are most commonly affected. OA represents a slow but efficient repair process (involving localised loss of cartilage and remodelling of adjacent bone) which results in a structurally altered but symptom-free joint. However, in some people, the process is inefficient (either due to overwhelming trauma or compromised repair ability) and this results in symptomatic OA. NICE recommends that an individual management plan should be agreed with each OA patient, taking into account co-morbidities that may affect that patient. **Education, exercise / physiotherapy, weight loss, use of suitable footwear (for shock absorbance) are core treatments in OA, irrespective of age or disability.** Patients may benefit from the use of walking aids, joint supports or special insoles. The use of heat / cold applications, or transcutaneous electrical nerve stimulation (TENS) should also be considered. **Pharmacotherapy:** Paracetamol is recommended as first line for pain relief; regular dosing may be required. Topical NSAIDs may be useful for OA of the knee or hand and should be considered ahead of oral NSAIDs or opioids. If NSAIDs/ COX-2 inhibitors are needed, they should only be used at the lowest effective dose for the shortest possible period. Co-prescribing with a proton pump inhibitor should be considered. If the patient is taking low-dose aspirin, analgesics other than NSAIDs should be considered first. Intra articular corticosteroid injection may be used for relief of moderate to severe pain, not responding to the above modalities. **Referral for surgical interventions** should be only considered in those whose QoL is substantially affected by refractory OA. Referral for arthroscopic lavage and debridement should not be routinely offered unless the OA patient has a clear history of mechanical locking. See [www.nice.org.uk/guidance](http://www.nice.org.uk/guidance) for further information and a management chart.



**High dose allopurinol toxic to skin** Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare life-threatening, bullous cutaneous conditions, generally considered to be immune-mediated reactions to drugs. They are thought to represent a single disease with common causes and mechanisms. Even although SJS and TEN are rare (2 cases/million/year), they are associated with high mortality (up to 25%) and morbidity. Medications including allopurinol, co-trimoxazole, phenobarbital, phenytoin, lamotrigine and carbamazepine have been implicated as causative factors in both SJS and TEN. The risk of allopurinol-associated SJS/TEN was evaluated in a recent study (*J Am Acad Dermatol 2008;58:25-32*). European patients (n=379) hospitalised with "community acquired" SJS/TEN were matched with 1505 hospitalised control patients from 6 countries. The data were adjusted for country, sex, age, exposure to known risk drugs for SJS or TEN, other drugs and suspected non-drug risk factors. The study found that **allopurinol was the commonest drug associated with SJS / TEN**; its use was recorded in 17.4% (n=66) of the SJS/TEN patients compared with 1.9% (n=28) of controls. **Doses of  $\geq 200$ mg allopurinol/day were associated with a 36-fold increased risk of SJS / TEN, while lower allopurinol doses were associated with a 3-fold increased risk.** The risk of SJS / TEN was restricted to recent users ( $\leq 8$  weeks between initiation of treatment and onset of reaction); there was no significant difference between the two groups and their total number of concomitant medications. The authors conclude that the study has shown that allopurinol, especially at high dose, is toxic to skin. They suggest that the incidence of allopurinol-associated SJS/TEN may be increasing because of increased use and increased dosage of the drug. [Editor's note: the starting dose of allopurinol is 100mg daily, which should be increased only if the serum urate response is unsatisfactory. Check out the full prescribing information for allopurinol at [www.medicines.ie](http://www.medicines.ie)].

*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](mailto:nmic@stjames.ie)*