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Update on MS. A recent paper reviewed the current knowledge regarding the aetiology and management of multiple sclerosis (MS) (*Lancet 2008; 372: 1502-17*). MS is a demyelinating disease associated with progressive damage and disability. It is primarily an **inflammatory disorder of the brain and spinal cord**. Focal lymphocytic infiltration leads to damage of myelin and axons, which initially is transient and focal in the majority of cases (=primary phase). New episodes occur erratically (generally <1.5 episodes/year) however, recovery from each episode is incomplete and eventually persistent symptoms accumulate (=secondary phase) and are associated with cumulative loss of axons. MS follows this course in around 65% of patients; in 20% the illness is progressive from onset. **Diagnosis** is based on the presence of clinical signs and symptoms indicating involvement of motor,

sensory, visual and/or autonomic systems; **MRI** shows focal or confluent abnormalities in white matter in >95% of patients. Few of the clinical features are classical apart from **Lhermittes' symptom** (electrical sensation of the spine or limbs on neck flexion) and **Uhthoff phenomenon** (transient worsening of symptoms and signs when body temperature increases e.g. after exercise). It is thought that **MS is triggered by environmental factors in individuals with complex genetic-risk profiles**. It is known that the risk of MS increases with distance from the equator. Many environmental triggers have been investigated including: Epstein-Barr virus / other viruses, air pollutants, cigarettes or other toxins, but results vary between studies. In addition MS has a familial recurrence rate of about 20%, however, the genetics appear to be complex and not yet fully understood. **Treatment:** In many cases the priority is to improve the quality of everyday life by **managing individual symptoms** such as bladder problems (with anticholinergics), pain (with carbamazepine, gabapentin), spasticity (with baclofen, benzodiazepines) and depression (with anti-depressants). Temporary improvement can be achieved during **symptomatic deterioration** with high-dose methylprednisolone. Plasma exchange up to one month after onset may reduce persistent deficits but not subsequent disease activity. Several therapies have been directed towards reducing disease activity: **β -interferons** (Avonex®, Betaferon® & Rebif®) and **glatiramer acetate** (Copaxone®) are licensed for use in relapsing-remitting disease and pivotal studies have shown reductions in the frequency of new episodes of disease of up to 30% with their use for up to 2-3 years compared with placebo. Interferons are associated with injection site reactions and flu-like symptoms; 5-30% of patients develop persistent neutralising antibodies, which lessen efficacy. Glatiramer is also associated with injection site reactions and care is needed when used in renal impairment. **Natalizumab** (Tysabri®) is an anti- α 4 integrin antibody directed against a lymphocytic surface antigen and studies showed a reduction in the relapse rate of 68% with one year's treatment and reduction in fixed disability by 42% over 2 year's treatment. However, it has been associated with the development of the potentially fatal **progressive multifocal leucoencephalopathy** when administered either as monotherapy or in association with a β -interferon. Therefore it is restricted to second line use as monotherapy in patients with severe relapsing remitting disease. The authors note that other anti-lymphocyte antibody agents and oral drugs are currently under development and they conclude that these, together with advances in the pathogenesis of MS should enable better understanding and management of the disease in the future.



Don't blame the sugar, blame the parents! A recent review article explored the belief that sugar causes hyperactivity in children (*BMJ 2008; 337:a2769*). Several double blind randomised controlled clinical trials have shown no effects on behavioural responses in children (both hyperactive and "normal" reactive) who received different levels of sugar (from sweets, chocolate as well as natural sources) compared with placebo. However, a study undertaken in mothers and their sons (aged 5-7 years and labelled behaviourally "sugar-sensitive") showed that, although all boys received a drink containing aspartame, mothers who believed their

sons had been randomised to receive a sugar drink, exercised more control over, and tended to be more critical of, their sons compared with the mothers who believed their sons were in the "placebo" group. The author suggests that the differences in the children's behaviour due to sugar were in the parents' minds!



Drugs and liver failure. The initial analysis of a US observational study of drug induced liver injury (DILI) was recently published (*Gastroenterology 2008;135(6):1924-1934*). DILI, which is the most common cause of death from acute liver failure in the US, is responsible for 13% of cases of acute liver failure. The risk factors and pathogenesis of DILI are poorly understood with most cases being unpredictable and believed to be an immunoallergic reaction or an abnormality in the metabolism of the agent. There is a growing awareness that non-prescription

drugs including herbal remedies and other OTC dietary supplements are also important causes of DILI. In the study, patients with suspected DILI were enrolled based on predefined criteria and followed up for at least six months. Patients with paracetamol associated liver injury were excluded. The initial analysis of the first 300 patients found that DILI was caused by a single prescriptive medication in 73% of cases, dietary supplements in 9% of cases, and either >1 medication or a combination of prescription and dietary supplements in 18% of cases. There were >100 different agents associated with DILI, with the major classes including: antimicrobials (45.5%), CNS agents including: antiepileptic agents, antidepressants, antipsychotics (15%), immunomodulatory agents (5.5%), analgesics (5%), anti-neoplastic agents (4%), anti-hypertensive agents (5%) and lipid-lowering agents (3.4%). **The most common single agents implicated were: co-amoxiclav (n=23), nitrofurantoin (n=13), isoniazid (n=13) and trimethoprim-sulfamethoxazole (n=13).** Causality adjudication assessed the likelihood of DILI as the reason for liver injury to be definite in 32%, highly likely in 41%, probable in 14%, possible in 10% and unlikely in 3%. Six months after enrolment, 14% of patients had persistent laboratory abnormalities and 8% had died, of which the cause of death was liver related in 44%. The authors concluded that DILI is caused by a wide variety of medications, herbal supplements and dietary supplements and that **antimicrobials represented the largest single class of agents that cause DILI which were responsible for >45% of cases.**



Antioxidants do not prevent cancer - further evidence.

Epidemiological studies have suggested that diets high in fruits and vegetables (which are rich with antioxidants) may prevent cancer, however findings from several randomised controlled trials (RCT) have been mostly negative. The results of another RCT, which evaluated the benefits and risks of antioxidants among women at high risk of cardiovascular disease in the primary prevention of cancer incidence and mortality, were recently published (*J Natl Canc Inst 2009; 101: 14-23*). A total of 7627 women, free of cancer at baseline, were included in the study and randomly assigned to either synthetic vitamin C, natural source vitamin

E, beta carotene or placebo and followed up for an average of 9.4 years. The results found that there were no statistically significant differences between the 4 groups on total cancer incidence or mortality. The authors concluded that supplementation with these antioxidants does not offer an overall benefit in the primary prevention of total cancer incidence or cancer mortality.



Reminder on Influenza. A recent press release from the Health Protection Surveillance Centre (HPSC) on the 18/12/2008 urged that people in high-risk categories should be vaccinated against influenza (flu) due to a doubling of numbers of flu-like illness cases reported in the previous week. Characterisation of the two Influenza A virus strains identified to date confirm they are included in the currently available vaccine. **High risk groups include:** those >65 yrs, people including children with severe illness such as chronic heart disease, chronic lung disease and diabetes, those with lower immunity due to disease or treatment, children with chronic arthritis requiring long-term aspirin therapy (because of the risk of Reye's

Syndrome), residents of nursing homes or other long stay facilities, health care workers and carers of those in high risk groups. The HPSC also advise that antiviral drugs are recommended for the prevention and treatment of flu in at-risk patients in line with NICE UK Guidelines. Full details are available on the HPSC's website (www.hpsc.ie).