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What is Antiphospholipid Syndrome (APS)? APS is a systemic autoimmune disorder characterised by vascular thrombosis, adverse outcomes in pregnancy and raised titres of antiphospholipid antibodies (APAbs), a heterogeneous group of autoantibodies directed at plasma proteins that bind to phospholipids (*BMJ 2010;340:c2541*). Primary APS (makes up >50% of cases) is estimated to affect 0.5% of the population; secondary APS is associated with other autoimmune diseases (including SLE of whom 30% develop APS). APS occurs mainly in young women of fertile age; only 12% of cases present at age >50 years (M>F) and APS is rare in children. **Clinical features** include: vascular thrombosis, pulmonary embolism, stroke, thrombotic endocarditis, migraine, myocardial infarction and obstetric manifestations. **Early recognition is crucial** as treatment can reduce mortality; however diagnosis is difficult due to a lack of standard diagnostic tests. **Current**

classification for APS requires at least one from each of the following clinical and laboratory criteria: vascular thrombosis (VT, ≥ 1 episode of arterial, venous or small vessel thrombosis in any tissue/organ); morbidity in pregnancy (≥ 1 unexplained death of a normal foetus at ≥ 10 wks' gestation, ≥ 1 premature birth of a normal neonate before 34 wks due to eclampsia/severe pre-eclampsia, or ≥ 3 unexplained consecutive spontaneous miscarriages at <10 wks); laboratory criteria (presence in serum/plasma on ≥ 2 occasions at least 12 weeks apart of: lupus anticoagulant or medium-high titres of either IgG / IgM anticardiolipin or anti- β_2 glycoprotein-I antibody).

Aetiology: the cause of development of APAbs, found in 1-5% of healthy subjects, is unknown. Influences include increasing age, chronic diseases, infections and certain drugs. APAbs affect the coagulation cascade and inflammation; an additional trigger/risk factor is thought to be required for the development of thrombosis. **The correlation between current APAbs and clinical symptoms is variable:** lupus anticoagulant is strongly associated with VT, stroke, foetal loss at >10 wks' gestation; anticardiolipin has high sensitivity but low specificity (a positive result has a stronger association with obstetric morbidity) and the clinical relevance of isolated anti- β_2 glycoprotein-I antibody is uncertain. The **risk of developing a clinical event** in apparently healthy people with persistently positive APAbs is unknown. Patients who are positive for all 3 APAbs are at high risk for pregnancy morbidity or thromboembolism; those with additional risk factors such as smoking and oral contraception are at additional risk. **Testing for APAbs is recommended** for patients experiencing unprovoked or recurrent thrombosis, morbidity in pregnancy and in patients with SLE.

Treatment: antithrombotic agents, to reduce the risk of recurrent thromboembolism, are the mainstay of treatment. Long-term anticoagulation with warfarin is recommended for a first episode of unprovoked venous thrombosis or thromboembolism associated with persistent positive APAbs (but may not be required for those with a reversible risk factor for thromboembolism). The level of evidence is low for preventing maternal thrombotic complications but several strategies have been proposed. Low molecular weight heparins are the agents of choice for antenatal thromboprophylaxis. A meta-analysis of intervention trials for recurrent early miscarriage concluded that heparin with low dose aspirin reduces pregnancy loss by 54%. There is a lack of evidence for those with a history of late miscarriage, foetal death and intrauterine growth restriction; most clinicians would consider treatment with low dose aspirin and heparin in these cases.

The article gives the following helpful **tips for non-specialists:**

- early recognition of APS helps prevent recurrent thrombosis and recurrent maternal and foetal morbidity
- all 3 laboratory tests should be performed (anticoagulants can influence the results of the lupus anticoagulant test)
- patients with positive results should be referred to a specialist
- pregnancies which are at high risk should be managed at specialised centres
- those with traditional risk factors for cardiovascular disease have increased risk of thrombosis with APS



New guidance on non-prescription codeine medicines. The Pharmaceutical Society of Ireland has issued guidance for pharmacists on the safe supply of non-prescription medicines containing codeine, which come into effect on 1st August. Codeine, a mild-moderate opioid, is available as a non-prescription medicine in analgesic preparations (often combined with paracetamol or ibuprofen) and in some cough remedies, as a cough suppressant. Because of its potential for misuse, it is classified as a "controlled drug" under the Misuse of Drugs legislation. The guidance lays out the legal and

professional considerations for the sale of codeine-containing medicines in Ireland to ensure safe use, and includes the following:

- codeine-containing medicines must only be supplied under the personal supervision of the pharmacist, who must satisfy him/herself that the supply is appropriate for, and in the best interest of, the individual seeking to buy such preparations
- the pharmacist must ensure that the individual seeking to buy these preparations is aware of potential adverse effects, interactions with other medicines etc and he/she should recommend that medical advice be sought if these medicines are not effective within a designated period (e.g. 3 days in the case of pain)
- the pharmacist must address the risks of prolonged use with the person prior to sale
- codeine-containing medicines must be stored in a safe site, under the supervision of the pharmacist and not accessible to the patient for self-selection; no advertising of any type (either in the window or within the pharmacy) is allowed for such medicines.

The full guidance document is available to download from: www.pharmaceuticalsociety.ie



Glucosamine (DONA®) not a "cost-effective therapy" for OA in Ireland. Osteoarthritis (OA) is the most common disease of the joints, and one of the most widespread of all chronic diseases. Symptoms can vary from minimal to severe pain and stiffness, but overall the disease is responsible for considerable morbidity. Increases in life expectancy and ageing populations are expected to make OA the fourth leading cause of disability by the year 2020.

Glucosamine is a natural substance found in mucopolysaccharides, mucoproteins and chitin. It is licensed in Ireland for the symptomatic relief of mild to moderate osteoarthritis of the knee. However, a review of the literature gives contradictory evidence for the efficacy of glucosamine for the treatment of OA. **Expenditure on glucosamine under the Community Drugs schemes in Ireland exceeded €9 million in 2008.** The National Centre for Pharmacoeconomics (NCPE) conducted an economic evaluation of glucosamine sulphate (DONA®) for the treatment of osteoarthritis in the Irish healthcare setting in June 2009 (www.ncpe.ie). The study investigated the cost-effectiveness of glucosamine sulphate 1500mg once daily as compared with placebo and paracetamol for treatment of OA of the knee. The review concluded "we do not believe that glucosamine sulphate (DONA®) is a cost effective therapy for the treatment of osteoarthritis in the Irish healthcare setting" and it recommended that reimbursement of the drug under the Community Drugs schemes should be reconsidered. The results of the NCPE review are consistent with those from expert groups in the UK: glucosamine is not recommended by either NICE (<http://guidance.nice.org.uk/cg59>) or the SMC (www.scottishmedicines.org.uk/smc/6099)

The challenge for good OA care is to assess each individual and consider the risks and benefits of treatment options based on reliable evidence. Current best practice recommends that all OA patients should have a comprehensive treatment plan to include both non-pharmacological and pharmacologic interventions, including **core treatments** such as education, physiotherapy and exercise; they may also benefit from specialist walking aids and support with weight loss. **Over half of OA patients report that pain, which may be persistent, is their worst problem.** This affects not only their mobility, but every aspect of their quality of life, therefore pain management is a key factor in the management of OA. Healthcare professionals should consider offering paracetamol for pain relief in addition to the core treatments; regular dosing may be required. **Paracetamol and/or topical NSAIDs should be considered ahead of oral NSAIDs, COX-2 inhibitors or opioids for pain relief in OA.**

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